# LAPAROSCOPIC STAGING IN CARCINOMA STOMACH AND ITS IMPACT ON TREATMENT PLAN


***A dissertation submitted to the Dr. M.G.R. Medical University, Tamil Nadu; in partial fulfillment of the requirement for the M.S. branch I (General Surgery) examination to be held in April 2014.***

# Certificate

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| Submission time | 15-Dec-2013 12:27PM |
| Total words | 9844 |

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LAPAROSCOPIC STAGING IN CARCINOMA STOMACH AND ITS IMPACT ON TREATMENT PLAN INTRODUCTION Gastric cancer ranks fifth among cancers in men and seventh among cancers in women in India. Geographic variation in distribution of gastric cancers is a known fact and is observed both worldwide and in India. Gastric cancer is a major problem in North-eastern and Southern states of India as seen in data from National Cancer Registry. According to the National Cancer Registry, age-adjusted incidence rate of stomach cancer in males was highest in Chennai (11.1 per 100,000) compared to 1.6 per 100,000 in Bhopal. There have been studies on the data collected by cancer registry on malignancies of affecting...

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**INTRODUCTION**

Gastric cancer ranks fifth among cancers in men and seventh among cancers in women in India. Geographic variation in distribution of gastric cancers is a known fact and is observed both worldwide and in India. Gastric cancer is a major problem in North-eastern and Southern states of India as seen in data from National Cancer Registry. According to the National Cancer Registry, age-adjusted incidence rate of stomach cancer in males was highest in Chennai (11.1 per 100,000) compared to 1.6 per 100,000 in Bhopal.

There have been studies on the data collected by cancer registry on malignancies of affecting gastrointestinal tract. These have shown that the incidence of gastric cancer is on the decline, this more marked in Delhi.

Stomach cancer ails from the fact that late presentation of symptoms brings patient to a doctor at advanced stages of the disease. The population-based survival studies have shown that despite improved treatment options, gastric cancer remains to have poor prognosis. This highlights the fact that appropriate investigative modalities for more accurate staging of the disease may contribute to better survival rates. Surgical resection remains the mainstay of treatment. Neoadjuvant, adjuvant, palliative chemotherapy form part of the multimodality treatment of this disease.

**ACKNOWLEDGEMENT**

I would like to express my gratitude to the following people without whom it would not have been possible to complete this dissertation.

My guide, Dr. Inian Samarasam, Professor of General Surgery, CMC Vellore, for his able guidance and help extended.

Dr. Anu Eapen, Professor Dept. of Radiology CMC Vellore for her help extended in reporting the CT scans.

Dr. Anna Pulimood ,Professor Dept. of Pathology, CMC Vellore and Dr. Dipti Masih, Assistant Professor Dept of Pathology, CMC Vellore for the help they extended as cytologists and reporting the cytology results.

Dr. Sudhakar Chandran, Dr. Vijay Abraham, Dr. Sam Varghese, Dr. Myla Yacob, Dept of General Surgery Unit III for their help.

My statistician, Ms Gouri for analyzing the data that was collected during the study.

All my teachers and colleagues in the Department of General Surgery for their encouragement and support.

All the patients who participated in the study.

My parents for all the support during the course of this project.

My wife Dr. Anu Alex for the support and help extended to me.

Last but not the least I thank God for the immense blessings he has showered on me.

# CONTENTS

# ABSTRACT

**TITLE OF THE STUDY** "Laparoscopic staging in carcinoma stomach and its impact on treatment plan"

DEPARTMENT : Department of General surgery Unit III

NAME OF THE CANDIDATE : Dr. Ashish Sam Samuel

DEGREE AND SUBJECT : M S General Surgery

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**OBJECTIVE**

Primary Objectives:

To study the efficacy of staging laparoscopy as compared to Computerized Tomography in assessing-metastatic disease (peritoneal and liver surface), T3 and T4 disease and location of primary tumor.

To study the role of staging laparoscopy in altering the management plan.

Secondary Objective:

To look at the role of peritoneal cytology

**METHODS**

This is a prospective study done among 66 consecutive patients diagnosed with adenocarcinoma stomach. Findings of both investigations were compared with final histopathology report. Peritoneal fluid aspiration cytology was done in all patients.

**RESULTS**

Of the 66 patients staging laparoscopy (SL) detected 23 patients with peritoneal metastases as against none by computed tomography (CT). SL detected 10 patients with ascites and 5 with liver surface metastases as against 6 patients with ascites and none with liver metastases by CT. There was a change in plan in 30 patients out of 66 patients recruited for the study (46%) based SL findings. T- Stage on staging laparoscopy shows fair agreement with gold (k=0.34, p=0.0004) so also the site of tumor was in agreement. Peritoneal fluid was positive in 7.58% by using the routine Papanicolaou staining.

KEY WORDS: Staging Laparoscopy, Peritoneal fluid Cytology, Computed tomography, Peritoneal disease-P1,P2,P3 , T3 and T4 disease, Liver Surface metastsis

## INTRODUCTION

Gastric cancer ranks fifth among cancers in men and seventh among cancers in women in India. Geographic variation in distribution of gastric cancers is a known fact and is observed both worldwide and in India. Gastric cancer is a major problem in North-eastern and Southern states of India as seen in data from National Cancer Registry.(1) According to the National Cancer Registry, age-adjusted incidence rate of stomach cancer in males was highest in Chennai (11.1 per 100,000) compared to 1.6 per 100,000 in Bhopal.(1) (2)

There have been studies on the data collected by cancer registry on malignancies of affecting gastrointestinal tract. These have shown that the incidence of gastric cancer is on the decline, this more marked in Delhi. (2)

Stomach cancer ails from the fact that late presentation of symptoms brings patient to a doctor at advanced stages of the disease. The population-based survival studies have shown that despite improved treatment options, gastric cancer remains to have poor prognosis. This highlights the fact that appropriate investigative modalities for more accurate staging of the disease may contribute to better survival rates. Surgical resection remains the mainstay of treatment.(3)(4) Neoadjuvant, adjuvant, palliative chemotherapy form part of the multimodality treatment of this disease.(5)

It needs to be stressed that optimum therapy can be offered only when tumor spread is accurately evaluated. The assortment of newer and sophisticated investigative modalities available presently like endoscopic and trans abdominal ultrasound, CT scan, MRI, PET-CT etc; have failed in accurately detecting peritoneal and occult surface liver metastases. Small volume

peritoneal involvement, occult liver metastases and lymph nodal involvement are still being detected only during surgery.(6) This has necessitated the need for an investigative modality that will pick peritoneal disease, disease involving liver surface and under surface of diaphragm. Laparoscopy stands out in its ability to look at these areas specifically.(7) Staging laparoscopy will hence possibly help in planning optimum treatment option. This study is designed to evaluate the role of diagnostic laparoscopy in staging of gastric cancer and to look at the change in treatment plan.

## RELEVANCE OF THE STUDY

Carcinoma of stomach is one of the important causes of cancer related deaths in India. Newly detected stomach cancers in India in year 2001 were 24985 among men and 11890 among women.(1) Mean annual age-standardized (world population) incidence of gastric cancer per 100,000 residents in India in 1990 was 9.7 for men and 4.7 for women.(1) Gastric carcinoma is often detected in its late stages in India. Surgical resection is the only potential curative treatment available. However, surgical resection is dependent on the staging of the disease.

Currently, Computerized Tomography (CT) is used as a routine preoperative tool for staging the disease. But CT Scan most often under-stages the disease as it does not totally exclude liver and peritoneal metastasis. Hence many patients undergo unnecessary laparotomy. Vistre et al., in 1988, reported that 25% of patients with gastric cancer underwent unnecessary laparotomy, and 13% to 23% developed complications due to the laparotomy.(8) This fact underlines the requirement of a better diagnostic tool, which can pick up advanced disease and avoid unnecessary laparotomy in already morbid individuals. Laparoscopic visualisation of the intraperitoneal organs will give a better staging of the disease extent and the metastatic involvement of the peritoneum and liver surface.(7) Various studies done show that laparoscopy is more sensitive than Computerized Tomography in detecting small volume peritoneal disease and liver surface involvement.(9) Other modalities like endoscopic ultrasound though effective in detecting early gastric cancers their sensitivity in detecting peritoneal disease is low.(10)(11) It is important that patients with incurable disease are not subject to radical surgery.

General Surgery unit III of CMC Vellore deals with upper GI surgeries and is high volume centre for gastrectomies. In year 2010-2011 the total number of inpatient admissions was 1059 of which 28% were of Upper GI specialty including gastric cancers. Of the total gastric surgeries done in 2010-2011, 138 were for carcinoma stomach. The patients who present to this centre come from varied geographical locations in India and therefore the results of the study may be applicable to any part of our country.

## AIMS AND OBJECTIVES

**AIM:**

To determine the role of staging laparoscopy in the staging of operable gastric adenocarcinoma and its impact on treatment plan

**OBJECTIVES:**

Primary Objectives:

- To study the efficacy of staging laparoscopy as compared to Computerized Tomography in assessing
    1. metastatic disease (peritoneal and liver surface)
    2. T3 and T4 disease
    3. Location of primary tumor
- To study the role of staging laparoscopy in altering the management plan.

Secondary Objectives:

1. To look at the role of peritoneal cytology

# REVIEW OF LITERATURE

## ANATOMY

The stomach is the most proximal abdominal organ of the digestive tract connecting the abdominal esophagus and the first part of duodenum.

## EXTERNAL FEATURES

The stomach has two surfaces: anterior and posterior, two curvatures: greater and lesser and two orifices- cardia and pylorus.

The cardiac orifice is attached to the lower end of esophagus. It lies behind left $7^{th}$ costal cartilage at the level of vertebra T11. Just proximal to the cardia at the gastro esophageal junction, there is a physiological sphincter, which controls reflux of acid into the duodenum. The pyloric orifice connects the stomach to the proximal duodenum. It lies half inch to the right of the median plane at the level of lower border of vertebra L1 in an empty stomach and in the supine position. Its position is indicated on the surface of stomach by a circular groove produced by the underlying pyloric sphincter and by the pre-pyloric vein which lies in front of the constriction.

The greater curvature is convex forming the left border of the stomach. It gives attachment to greater omentum, the gastrosplenic ligament and gastrophrenic ligament. It presents a cardiac notch at its upper end which separates it from the esophagus.(12)

The lesser curvature is concave forming the right border of the stomach. It gives attachment to the lesser omentum. Angular notch or incisura angularis marks the most dependant part of the curvature.

The anterior surface faces forwards and upwards and the posterior surface faces backwards and downwards.

**LANDMARKS**

Topographically, the stomach is divided into regions: the cardia and gastro-esophageal junction, the fundus, the body or corpus, the antrum, and the pylorus.

The fundus is the superior most part of the stomach. The angle of His is where the fundus meets left side of the GE junction.

The body of the stomach is the largest region. The inferior extent of the fundus is considered to be the horizontal plane of the GE junction, where the body starts.

The antrum begins at the incisura angularis where the lesser curvature turns abruptly to the right. It comprises distal 25 to 30% of the stomach.

The fundus and corpus harbor acid-secreting glands, whereas the antrum harbors alkaline-secreting surface epithelium and endocrine, Gastrin secreting G-cells.

On endoscopy, the GE junction is distinguished by the transition between the flat, pale, stratified epithelium of the esophagus and the lush, pink, glandular epithelium of the upper stomach. The junction between the acid-secreting corpus and the non-acid secreting antrum is also distinguished by the rugal pattern. Those of the antrum are linear and aligned with the

long axis of the organ, whereas those of the corpus are convoluted and oriented obliquely. The pylorus is visualized, outlined by the underlying ring of muscularis.(12)

**RELATIONS**

**PERITONEAL RELATIONS**

Both the surfaces of stomach are lined by peritoneum. Layers of the peritoneum meet at the lesser curvature and become continuous with the lesser omentum. The two layers meet along the greater curvature to form the greater omentum. The two layers meet to form the gastro-splenic ligament near the cardiac end of the greater curvature. On the posterior surface near the cardiac end the peritoneum is reflected on to the diaphragm as the gastro-phrenic ligament. Above this ligament a small part of the posterior surface of stomach is in direct contact with the left crus of diaphragm and is called the bare area of the stomach.

**VISCERAL RELATIONS**

Liver, diaphragm and the anterior abdominal wall forms the anterior relations of the stomach. Posterior surface is related to structures which form the stomach bed such as the diaphragm, left kidney, left suprarenal gland, pancreas, transverse mesocolon, splenic flexure of the colon and the splenic artery.

**BLOOD SUPPLY**

**ARTERIAL SUPPLY**

The stomach is supplied by 1) the left gastric artery, a branch of the celiac axis, which supplies the cranial portion of the lesser curvature. 2) The right gastric artery, a branch of the common hepatic artery, which supplies the caudal portion of the lesser curvature. 3) The right gastroepiploic artery, a branch of the gastroduodenal artery, which supplies the antrum and lower body. 4) The left gastroepiploic artery, a branch of the splenic artery, which supplies the upper body and (5) a series of short gastric arteries, which are branches of splenic artery supply the fundus and cranial portion of the body.

**VENOUS SUPPLY**

Right and left gastric, right and left gastroepiploic and short gastric veins of the stomach drain into the portal vein directly or via the superior mesenteric vein or splenic vein.

**NERVE SUPPLY**

Extrinsic sympathetic nerve supply is derived from segments T5 to T10 via the splanchnic nerves to celiac ganglion. Post ganglionic sympathetic nerves then travel from celiac ganglion to stomach along the blood vessels.

Extrinsic parasympathetic nerve supply is derived from the vagus nerves which forms the esophageal plexus. This esophageal plexus above the hiatus forms the left anterior and right posterior vagal trunks. Anterior vagus sends branches to the liver in gastro hepatic ligament and travels along the lesser curvature as the anterior nerve of Latarjet. It gives branches to the body of stomach and terminates near the incisura angularis as the crow's foot and give branches to antropyloric region. Posterior vagus send branches to the celiac plexus and continues along the posterior lesser curvature. The branch that the posterior vagus sends to the posterior fundus is called as the criminal nerve of Grassi.

Neurons in the myentric and sub mucosal plexuses form the intrinsic nervous system of the stomach.

**LYMPHATIC DRAINAGE**

Lymphatics of the stomach run in close proximity to blood vessels. The cardia and medial half of the body drain into nodes along the left gastric and celiac axis. The proximal greater curvature of the stomach drains into nodes along the left gastro-epiploic or splenic hilum. Greater curvature half of the distal stomach drains into nodes along the right gastro-epiploic hilum. The lesser curvature side of the antrum drains to the right gastric and pyloric nodes. The nodes along both the greater and lesser curvature commonly drain into the celiac nodes. There is a rich anastomosis of lymphatics that drain the stomach.

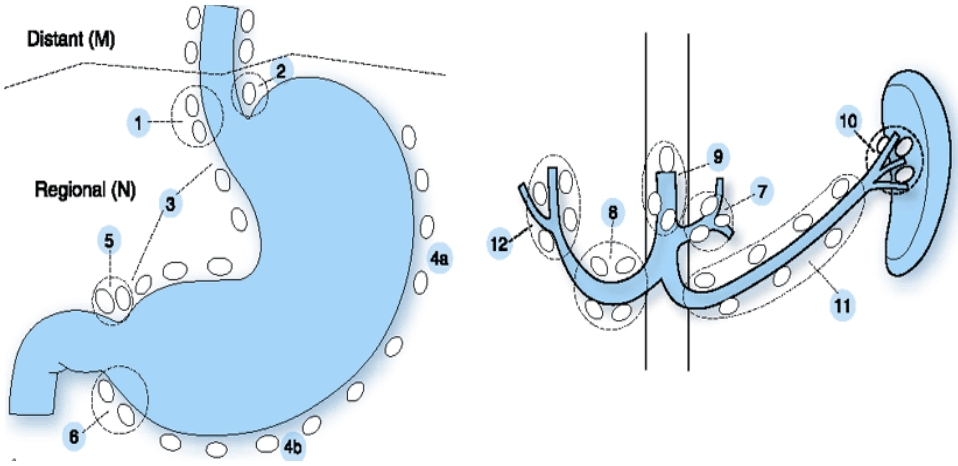


Figure 1: Lymph node stations in gastric carcinoma

(1) Right cardiac (2) left cardiac (3) lesser curve (4) greater curve (5) supra-pyloric (6) Sub pyloric (7) left gastric artery (8) common hepatic artery (9) coeliac artery (10) splenic hilum (11) splenic artery (12) hepatoduodenal

Sixteen lymph nodal stations have been identified according to the Japanese Research Society for the study of Gastric Cancer (JRSGC) for the purposes of staging of gastric carcinoma.(13)

Stations of nodal spread in gastric cancer according to the system of the Japanese Research Society of study of Gastric Cancer along with their designations as local (R1), regional (R2) or distal-regional (R3) spread

| STATION | LOCATION | ANTRUM | BODY/FUNDUS |
|---|---|---|---|
| 1 | RIGHT CARDIA | R2 | R1 |
| 2 | LEFT CARDIA | R2 | R1 |
| 3 | LESSER CURVE | R1 | R2 |
| 4 | GREATER CURVE | R1 | R2 |
| 5 | SUPRAPYLORIC R.GASTRIC A. | R1 | R2 |
| 6 | INFRAPYLORIC | R1 | R2 |
| 7 | L.GASTRIC A. | R1 | R1 |
| 8 | COMMON HEPATIC A. | R2 | R2 |
| 9 | CELIAC AXIS | R3 | R3 |
| 10 | SPLENIC HILUM | R3 | R1 |
| 11 | SPLENIC A. | R3 | R1 |
| 12 | HEPAODUODENAL LIG. | R2 | R1 |
| 13 | PANCREATIC HEAD | R2 | R2 |
| 14 | ROOT OF SMA | R3 | R3 |
| 15 | MIDDLE COLIC A. | R3 | R3 |
| 16 | PARA AORTIC | R3 | R3 |

Table1: Lymph node stations in gastric carcinoma(13)

**RISK FACTORS FOR CARCINOMA STOMACH**

| | |
|---|---|
| Infections | Helicobacter pylori |
| | Epstein bar virus |
| Diet | High salt intake |
| | Nitrites and nitrates |
| | Low intake of fruits and vegetables |
| Pernicious anemia | |
| Habits | Smoking |
| | Alcohol consumption |
| Gastric surgeries | Stump carcinoma |
| Peptic ulcer disease | |
| Ionizing radiation | |
| Hereditary factors | Blood group A |
| | Gastric polyps |
| | Hereditary diffuse gastric cancer |
| | Hypertrophic gastropathy |

Table 2: Risk factors for carcinoma stomach(14)

## CLINICAL FEATURES OF GASTRIC CANCER

The symptoms of stomach cancer tend to be vague and nonspecific hence eluding early detection. This can be attributed to the fact that both the organ in question and the cavity that contains it are accommodative to distention. Gastric cancer share early symptoms with benign disease. This prevents the patient and the treating doctor to be more cautious of the symptoms. Outside of Japan, screening for gastric cancer is not performed. . Even in industrialized countries like The United States Of America, it is quite common for patients to be misdiagnosed with disease of benign etiology and to have undergone treatment for the same before realizing the folly.

According to Paul F. et al the most common symptoms and there frequency of occurrence is as follows:

| SYMPTOM | FREQUENCY |
|---|---|
| Abdominal pain | 50 to 60% |
| Weight loss | 40% |
| Overt upper gastrointestinal bleed | 16 to 17 % |

Table 3: Symptoms in gastric cancer and their frequency of occurrence(15)

The same investigators have analyzed over one thousand cases of stomach cancer at M. D. Anderson Centre and have found that many of the symptoms are site specific. Dysphagia was seen more commonly in proximal tumors while distal tumors had vomiting and nausea as prominent symptoms. Patients with linitis plastica most commonly presented with early satiety.(15)

Physical examination may reveal the stigmata of the disease but most often these are indication of progression of the disease. Jaundice, palpable intra abdominal mass, free fluid, left supra clavicular lymphadenopathy, umbilical nodule, Blummer shelf nodules are indications of advanced disease.

## DIAGNOSIS

Carcinoma stomach is one of the commonest reasons for oncological death in our country. Early detection and treatment of the same is paramount. Gastric cancer remains to have only surgery as the potentially curative treatment. Therefore the disease needs to be adequately staged for optimum treatment. In patients who are suspected with carcinoma stomach investigations are directed towards - Diagnosis and Staging of the disease.

Diagnosis is usually using endoscopy and biopsy. Patients who present with symptoms suspicious of carcinoma stomach undergo upper gastrointestinal endoscopy and biopsy from the lesion.

Various staging options are available. Endoscopic ultrasonography and multidetetector computed tomography are presently in vogue.

### UPPER GASTRO INTESTINAL ENDOSCOPY AS A DIAGNOSTIC TOOL IN CARCINOMA STOMACH

Upper gastrointestinal endoscopy is the diagnostic tool most commonly employed in gastric malignancies. British consensus guidelines recommends that the gastric cancer is diagnosed by seeing the lesion on endoscopy and confirming diagnosis by histo pathological examination of minimum six tissue biopsy from the lesion. If there the biopsy results of suspected lesion are inconclusive then a repeat biopsy is warranted.(16)(17)

Of late there has been a surge of technological innovations in the field of gastrointestinal endoscopy. This has helped in detecting more number of early gastric cancers. Chromo endoscopy using indigo dye spraying helps in identifying early gastric cancer. Magnifying endoscopy with narrow-band imaging (NBI) helps in visualizing micro vascular observation of the micro vascular architecture of the mucosa and micro surface pattern of the tumor. Endo cytoscopy helps in visualizing the cell itself and even the nuclei.(18)(19) All these have helped in identifying early gastric cancer but the crux of the matter is late presentation of the disease in our country. Majority of the time the disease is beyond the scope of endoscopic therapeutic interventions. Easy availability, the simplicity of the procedure, the possibility to biopsy the lesion and the cost effectiveness of the procedure entail it to remain as the first port of call in the diagnosis of carcinoma stomach.(16)

**ENDOSCOPIC ULTRSONOGRAPHY AS A STAGING MODALITY IN CARCINOMA STOMACH**

Gastric carcinoma appears hypoechoic on endoscopic ultrasound. This modality has its importance in the fact the early gastric cancers are now being treated by endoscopic mucosal resection. However the purview of this modality does not extend beyond T1 and T2 disease. Endoscopic ultrasound may underestimate the depth of invasion by the tumor and overestimate lymph nodal involvement due to inflammatory process around the nodes. However distant nodal metastases are difficult to be detected on endoscopic ultrasound. (11)(20)

**COMPUTED TOMOGRAPHY IN STAGING OF CARCINOMA STOMACH**

The most commonly performed and widely available one is computerized tomography. The overall accuracy of transverse CT and volumetric CT for tumor staging is 77% and 84% respectively.(21) It has been noted that extraserosal involvement and metastases are difficult to be precisely detected on CT. The tumor staging of disease, especially T3 and T4 is a challenge as it is hard to distinguish fat stranding around the tumor as due to infiltration or inflammation. Peritoneal carcinomatosis is another condition which the computerized tomography does not detect when in small volumes.

In a review done by R.Hargunani et al, detection and staging of gastric neoplasia using multi detector computed tomography and endoscopic ultra sound was studied. MDCT aids the detection and radiological staging of gastric carcinoma when it is combined with multi planar reconstruction the accuracy of T stage determination improves to 89 per cent as compared with axial images alone which is 73 per cent.(22) However endoscopic ultrasound has a better diagnostic rate of 74 to 94 per cent in determination of T stage.(22) But EUS is more invasive and distant nodal disease and metastases are difficult to be picked up .It has its own advantage of being useful in the therapeutic management of early gastric cancer (when the lesions are confined to mucosa and sub mucosa endoscopic mucosal resection is a possibility). Nodal staging in gastric cancer is a challenge whatever the technique used. Enlarged nodes detected by either EUS or CT may subsequently be proven to be inflammatory; on the contrary normal sized nodes may be metastatic. EUS can potentially detect metastases in liver, mediastinum and

even peritoneum. However, it is not primarily employed for detection of distant disease. CT remains the initial method of choice.

In a similar study by Chiao-Yun Chen, the accuracy for peritoneal involvement was 96 per cent using multi detector computed tomography. This study did not look at the accuracy of transverse CT in detecting peritoneal disease.

In a study of 63 patients using MDCT and EUS by Suryaprakash Bhandari, et al; the accuracy of lymph node staging was 75 per cent for MDCT and 79 per cent for EUS.(23) D'Ugo DM, et al found that the sensitivity of computerized tomography for T3 and T4 disease was 23.2% and 48.3%, respectively. 21 out the 100 patients who underwent laparoscopy had metastasis which not detected on preoperative staging CT.(24)

Gonzale-Moreno S et al studied the effectiveness of computed tomography in the detection of peritoneal carcinomatosis. Even with improvements in technology and availability of contrast-enhanced, multi detector computed tomography, the early detection and characterization of peritoneal disease is a major challenge. Often small volume peritoneal implants remain undetected. Even so contrast-enhanced, multi detector computed tomography is the mainstay in detection of peritoneal disease.(25)

Sung Wook Hwang et al In 277 patients with gastric cancer endoscopic ultrasound and computed tomography were done as part of operative evaluation. Results of pre operative endoscopic ultrasound and MDCT were compared to post operative histopathological findings. The overall accuracy of EUS and MDCT for T stage was 74.7 per cent and 76.9 per cent respectively. Similarly the overall accuracy for N stage was 66 per cent and 62.8 per cent

respectively. However this study did not look to the aspect of peritoneal and liver surface metastases.(26)

Therefore there is need for better diagnostic tool for peritoneal disease. According to National Comprehensive Cancer Network (NCCN) guidelines 2011, following protocol is followed.

| | |
|---|---|
| Tis/T1a, medically unfit | Endoscopic mucosal resection(EMR) and endoscopic surveillance |
| Tis/T1a, medically fit | EMR or Surgery |
| Potentially resectable, medically fit , M0 | Surgery or Preoperative chemotherapy followed by surgery |
| Potentially resectable, medically fit , M1 | Palliative therapy |
| Unresectable tumors, medically fit, M0 | Chemoradiation(definitive) |
| Unresectable tumors, medically fit, M0 | Palliative therapy |
| Medically unfit M0 | Chemoradiation(definitive) |
| Medically unfit M1 | Palliative therapy |

Table 4: NCCN guidelines for treatment in carcinoma stomach

Hence according to NCCN guidelines laparoscopy can be considered in resectable or unresectable M0 disease.(27)

**ROLE OF POSITRON EMISSION TOMOGRAPHY**

This modality uses difference in metabolic activity between normal tissues and tumor tissues in identifying the disease. Positron emission tomography uses the property of increased glycolytic activity of the tumor tissues and they metabolize fluoro-2-D-glucose at higher rate than normal tissues. The results with PET are a mixed bag. There are studies which have quoted sensitivity of 93% in detecting the primary lesion in gastric carcinoma. However it is found that in approximately 20% of patients with gastric cancer, the primary tumor is not detected by PET. The reason for the above phenomenon is due to the fact that poorly differentiated and mucinous carcinomas are not PET avid. It is also found that nodal assessment by this modality is poor.(25)

**ROLE OF LAPAROSCOPIC STAGING IN CARCINOMA STOMACH**

Laparoscopic staging is the use of a fiber optic laparoscope to determine the extent of involvement by a malignant tumor within the peritoneal cavity.

HISTORICAL PERSPECTIVE

Laparoscopy was first described by the beginning of 20th century. Interestingly it was first promoted as an adjunct in diagnosing diseases in the abdomen. It gained foothold as a therapeutic tool among general surgeons only by 1986 when it was used for laparoscopic cholecystectomy .Newman of Glasgow modified the Edison's electric bulb so that it could b mounted on a cystoscope. Georg Kelling is credited with performing a laparoscopic surgery in dogs. In human it was first attempted by Jacobaeus of Sweden. Benedict of Boston used laparoscopy in diagnosis of liver disease, ascites, cancers of stomach and colon. It was Waugh from Mayo Clinic who first reported that laparoscopy was the best tool to assess ascites and the accuracy rate with which laparoscopy diagnosed intraabdominal malignancy was 93%.(28)

COMPLICATIONS OF LAPAROSCOPY

Laparoscopy is a fairly safe procedure. The complications encountered can be divided as following:

1. Complications related to access
2. Complications of pneumoperitoneum
3. Complications of surgical procedure per se

ACCESS RELATED COMPLICATIONS

Jansen et al found that 57% of complications in gynecological cases were related to insertion of trocar. Problems associated with access account for 0.3% complications and they include major injuries to retroperitoneal vessels and to the bowel.(29) A study conducted by Mayol et al showed that there was 5% complications related with access(29) and they included –

1. Abdominal wall hematoma (2%)
2. Umbilical hernia (1.5%)
3. Umbilical wound infection (1.2%)
4. Penetrating injuries (0.2%)

However the rate of complications related to access can be reduced by using open technique of entry.

PNEUMOPERITONEUM RELATED COMPLICATIONS

Study conducted by Patel et al found the patients undergoing laparoscopic cholecystectomy were at high risk of developing deep vein thrombosis. The pneumoperitoneum decreases cardiac output by up to 30% and mean arterial pressure increases in 16% of cases.(29) However the duration of pneumoperitoneum in staging laparoscopy is less and the ill effects of pneumoperitoneum on the cardiovascular system can be ameliorated by preloading with isotonic fluid and by keeping the patient in supine position as much as possible. However, due to the short duration of the procedure, such problems due to pneumoperitoneum are very rare.

COMPLICATIONS OF SURGICAL PROCEDURE PER SE

Since there is no major handling of viscera involved in staging procedure, visceral injuries are quite far and in between. The major complications occurring are the off camera injuries. These are minimized with experience of the surgeon.

NEED FOR LAPAROSOPIC STAGING

There have been many prospective and retrospective studies in this regard. D Mahadevan et al conducted a prospective study involving 40 patients from 2006 to 2008 to assess the value of preoperative laparoscopic staging for gastric cancer. Histopathological examination was considered gold standard for the staging. This was compared with CT and laparoscopy. Most significant finding of the study was that laparoscopy detected 7 cases of peritoneal metastases which were not picked on CT. Hence these patients were saved the morbidity and mortality associated with unnecessary laparotomy. In this study assessment of T factor was quite variable .While T3, T4 disease could be easily assessed, lesions less than T3 were difficult to be assessed laparoscopically. Sensitivity of laparoscopy for T3 tumors were 90.3 per cent as against 58 per cent for CT. Hence this study concluded that laparoscopy is sensitive in detecting peritoneal metastases and helped in avoiding unwanted laparotomy.(8)

Andronik Kapiev et al conducted a retrospective study on 361 gastric cancer patients. All patients in this study underwent a CT preoperatively. Patients with T4 disease or un-resectable disease were excluded from the study. Diagnostic laparoscopy was performed on these

patients. They found that 23 of 28 patients had peritoneal spread undetected on CT. They concluded that diagnostic laparoscopy has to be considered in all stomach cancer patients who will be undergoing curative resections.(30)

Between January 2006 and December 2008 a prospective study was conducted by Valentin Muntean et al. They looked at laparoscopy and laparoscopic ultrasonography in accurate staging of alimentary tract cancers. In their study unnecessary laparotomies were avoided 36.4 per cent of patients. These patients did not have distant metastases on pre operative staging imaging. The overall morbidity for staging laparoscopy was 2.45 per cent and they had no mortality. In this study they also looked the value of laparoscopic ultrasound and peritoneal cytology. This study included esophageal, gastric, hepatobiliary, pancreatic and colorectal malignancies. They concluded that staging laparoscopy can avoid unnecessary laparotomies in all these malignancies and aid in faster recovery and earlier time to adjuvant treatment in which laparotomy was avoided.(31)

Gian Carlo Roviaro et al studied 83 patients from 1994 to 1999 with gastric cancer. 71 of 83 patients underwent laparoscopic staging. All of these patients had preoperative staging with computed tomography. In their series laparoscopy accuracy for T3 lesion reached 88.5% and T4 81.2%. In 6 out 71 patients laparoscopy revealed causes for unresectable tumors and hence avoided unnecessary laparotomy.(32)

IS STAGING LAPAROSCOPY REUIRED FOR ALL PATIENTS WITH CARCINOMA STOMACH?

Staging laparoscopy is useful in the detection of peritoneal disease and the likelihood of peritoneal spread is very small when there are T1 or T2 lesions. There is evidence to say that staging laparoscopy not necessary in early disease.

Staging laparoscopy is recommended in following scenarios

1. Whenever Neoadjuvant treatment is planned upfront.
2. In T3 and T4 disease (the likelihood of peritoneal disease in T1 and T2 disease is very low). .
3. Laparoscopic staging provides opportunity to obtain peritoneal fluid for cytology.

Lehnert et al studied 120 patients with adenocarcinoma of stomach of which 96 patients had laparotomy upfront with curative intent in 81 and palliative intent in 15 patients. In two of the patients out of 81 planned for curative resection laparotomy was abandoned due to peritoneal metastases. Fifteen patients underwent laparoscopic staging primarily. Peritoneal metastasis was observed in six patients and the other four did not have peritoneal involvement. He concluded that diagnostic laparoscopy is not warranted for all cases of adenocarcinoma of stomach.(33)

## PERITONEAL FLUID CYTOLOGY

Peritoneal fluid cytology is helpful in prognosticating gastric carcinoma. The impact of peritoneal cytology is evident in the fact that it has been included in the present AJCC staging as M1 disease. Therefore it is used as an adjutant in staging of gastric cancer. Several studies have shown that there is reduced survival when cytology is positive. Presence of malignant cells in peritoneal lavage has been reported in the range of 6.8 to 23 percent. James J. Mezhir et al conducted a prospective trial to ascertain the value of diagnostic peritoneal lavage in detecting positive peritoneal fluid. They found that 12 patients of the 22 had positive cytology which was 4.5 per cent.(34) In a review done by Martin R et al, it has been noted that the likelihood of finding tumor cells in a cytology specimen appears to be related to the tumor stage of the disease. The review further notes that when the cytology uses Papanicolau method there is no patients with T1 and T2 disease who have positive cytology. The cytology positivity rate was 10 percent in T3 and T4 disease and 59 percent in M1 disease. However the sensitivity increases if immunohistochemistry or reverse transcriptase polymerase chain reaction is used.(16) If we look in detail into these studies one will find that cytology can be positive even in T1 or T2 disease especially when immunohistochemistry or reverse transcriptase reaction technique is employed. In a study conducted by Martin J.K Jr et al, abdominal fluid cytology in 76 patients with various gastro intestinal malignant lesions was looked into. 43 per cent of patients with gastric cancer were found to have positive tumor cells in their peritoneal washings. They found tumor cells in early malignancies.(16)

Based on the current TNM 7 recommendations, where peritoneal disease is staged as M1 disease, it is essential to look at the cytology in the pre operative staging of gastric cancer.

PAPANICOLAU STAIN IN PERITONEAL FLUID CYTOLOGY

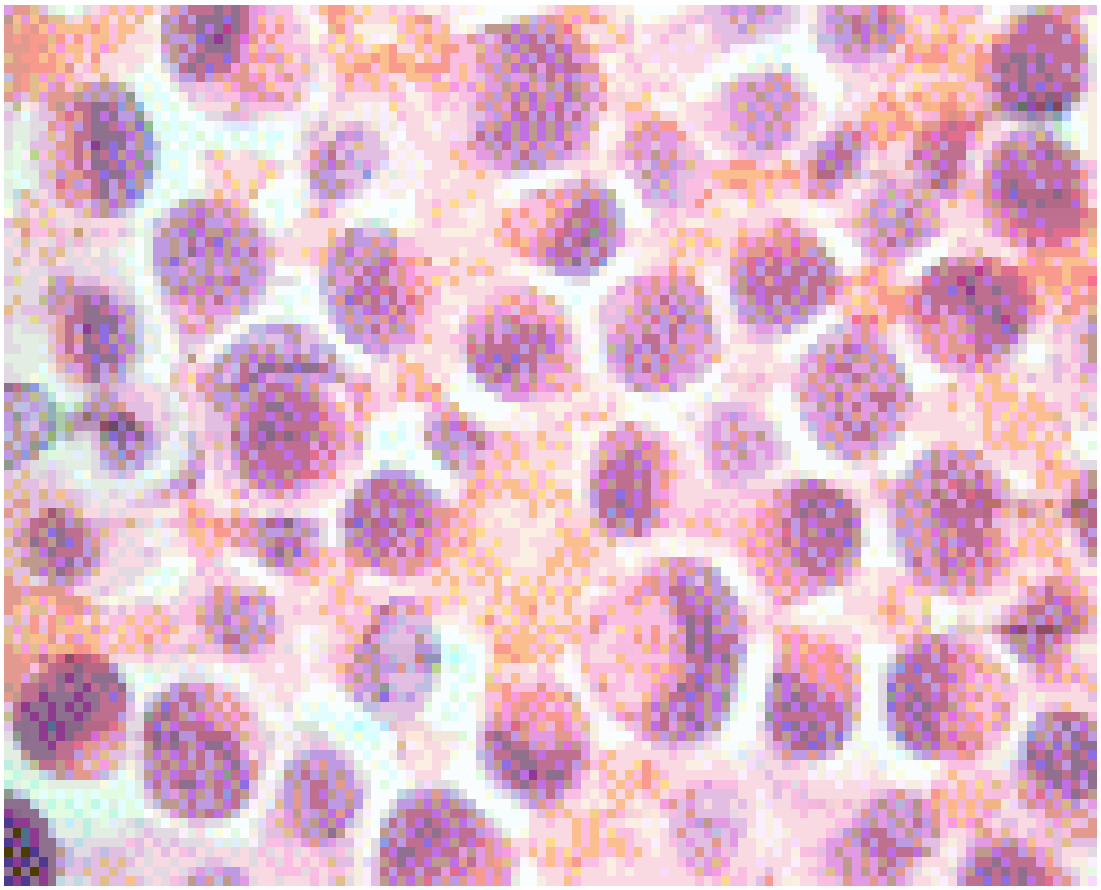

Figure 2: Papanicolau stain in peritoneal fluid cytology

STAGING OF GASRIC ADENOCARCINOMA ACCORDING TO UICC/AJCC STAGING (7TH EDITION)

| PRIMARY TUMOR T | |
|---|---|
| TX | PRIMARY TUMOR CANNOT BE ASSESSED |
| T0 | NO EVIDENCE OFPRIMARY TUMOR |
| Tis | CARCINOMA INSITU |
| T1 | TUMOR INVADES LAMINA PROPRIA /MUSCULARIS MUCOSAE/SUBMUCOSA |
| T1a | TUMOR INVADES LAMINA PROPRIA /MUSCULARIS MUCOSAE |
| T1b | INVADES SUBMUCOSA |
| T2 | INVADES MUSCULARIS PROPIA |
| T3 | PENETRATES SUBSEROSAL CONNECTIVE TISSUE WITHOUT INVASION |
| T4 | INVADES SEROSA - |
| T4a | VISCERAL PERITONEUM |
| T4b | ADJACENT STRUCTURES |
| REGIONAL LYMPH NODES N | |
| NX | CANNOT BE ASSESSED |
| NO | NO REGIONAL NODE METS |
| N1 | 1TO 2 REGIONAL NODES INVOLVED |
| N2 | 3TO6 |
| N3 | 7 OR MORE |
| N3a | 7 TO 15 |
| N3b | 16 OR MORE |
| DISTANT METASTASIS M | |
| MO | NO DISTANT METASTASIS |
| M1 | DISTANT METASTASIS |

Table 5: Staging of gasric adenocarcinoma according to UICC/AJCC staging

| | | | |
|---|---|---|---|
| STAGE O | Tis | N0 | M0 |
| STAGE 1A | T1 | NO | M0 |
| STAGE 1B | T2 | N0 | M0 |
| | T1 | N1 | M0 |
| STAGE IIA | T3 | N0 | M0 |
| | T2 | N1 | M0 |
| | T1 | N2 | M0 |
| STAGE IIB | T4a | N0 | MO |
| | T3 | N1 | M0 |
| | T2 | N2 | MO |
| | T1 | N3 | MO |
| STAGE IIIA | T4a | N1 | M0 |
| | T3 | N1 | M0 |
| | T1 | N3 | M0 |
| STAGE IIIB | T4b | N0 | MO |
| | T4b | N1 | MO |
| | T4a | N2 | M0 |
| | T3 | N3 | M0 |
| STAGE IIIC | T4b | N2 | M0 |
| | T4b | N3 | M0 |
| | T4a | N3 | M0 |
| STAGE IV | ANY T | ANY N | M1 |

Table 6: Stage grouping in carcinoma stomach

## TREATMENT OPTIONS

### ADJUVANT CHEMORADIOTHERAPY

### MACDONALD'S TRIAL

Curative surgical resection alone would not be adequate to prevent recurrence in adenocarcinoma of the stomach. Macdonald's trial in 2001 looked into the effectiveness of surgery plus postoperative chemoradiation in adenocarcinoma of stomach. In the surgery-only group the median overall survival was 27 months, as compared with 36 months in the surgery plus chemoradiotherapy group. They concluded that adjuvant chemoradiotherapy should be instituted in all those who have increased for recurrence of gastric adenocarcinoma.(35)

### ARTIST TRIAL

In this trial chemoradiotherapy was compared with chemotherapy as an adjuvant treatment option. 458 patients who had completely resected tumors were included in this study. Patients were randomized into two arms one in whom Capcitabine and Cisplatin were given the other group received radiotherapy along with afore said chemotherapy regimen. 75.4% patients completed treatment in chemotherapy only arm and 81.7% completed treatment in chemoradiotherapy arm. The addition of radiation to chemotherapy did not change the disease free survival (p=.0862) but chemoradiotherapy arm saw better outcomes with those with node positivity which was statistically significant. This significance was maintained in a multivariate

analysis. The estimated hazard ratio in this sub group was 0.6865and 95% confidence interval of 0.4735 to 0.9952. (36)

ADJUVANT CHEMOTHERAPY

S1 TRIAL

This was Japanese randomized control trial where oral fluoropyrimidine derivative S-1 was used as adjuvant chemotherapeutic agent. In 2011 the 5 year follow up report was published. They found that in whom gastrectomy with D2 lymphadenectomy was done when Adjuvant agent S-1 added the overall survival rate increased to 71%as against 61.1% in surgery alone group. They also noticed that adding the adjuvant agent S-1 increased the relapse free survival rate at 5 years to 65.4% as against 53.1% in surgery only group.(37)

**CLASSIC TRIAL**

This was an eastern trial looking into the benefits of adjuvant chemotherapy. They studied the effects of giving Capcetabine and Oxaliplatin after D2 gastrectomy and surgery alone in 1035 patients with stage II and III disease. At a median follow-up of 34 months, chemotherapy was associated with a significant improvement in three-year disease-free survival, with only a borderline statistically significant improvement in overall survival (83% versus 78 %). However,

with longer follow-up they could show that there was improvement in overall survival with chemotherapy. This was statistically significant (five-year overall survival 78% versus 69 %). (38)

## NEOADJUVANT CHEMOTHERAPY

### MEDICAL RESEARCH COUNCIL ADJUVANT GASTRIC INFUSIONAL CHEMOTHERAPY (MAGIC) TRIAL

Between 1994 and 2002 a major trial in United Kingdom created a paradigm shift in the way we viewed the treatment of gastric cancer. The United Kingdom National Cancer Research Institute (NCRI) conducted the Medical Research Council Adjuvant Gastric Infusional Chemotherapy (MAGIC) trial which recruited 503 patients over eight years. This was the first randomized trial of its kind which conclusively demonstrated a survival benefit by using perioperative chemotherapy in those who had resectable adenocarcinoma of the stomach, gastro esophageal junction, and lower esophagus, compared with surgery alone. This trial used the ECF regimen for perioperative chemotherapy which included Epirubicin, Cisplatin and continuous infusion 5-fluorouracil. The five year survival rate in the intention-to-treat (ITT) analysis was 36%. The study showed that in comparison patients treated with surgery alone had a five year survival rate of 23%. This study also showed that there was significant improvement in Progression-free survival with perioperative chemotherapy (hazard ratio for progression, 0.66; 95% confidence interval, 0.53–0.81; P <.001). This trial has downsides to it. This study was open to recruitment

during 1994 to 2002. The downsides to this trial are that t patients did not have detailed preoperative staging of the disease. The surgery done was not standardized and chemotherapy commencement and completion rates were poor. (39)

FRENCH MULTICENTER TRIAL (**FNLCC/FFCD)**

This trial was conducted to look at the effect of perioperative chemotherapy on overall survival in those who have undergone curative resection for gastric and esophageal adenocarcinoma. This trial made use of 5- fluorouracil and Cisplatin as chemotherapeutic agents. It was found that those who had perioperative chemotherapy had 35 percent reduction in the risk of disease recurrence. They also experienced significant reduction in the risk of death (31% reduction).

EUROPEAN ORGANISATION FOR RESEARCH AND TREATMENT OF CANCER RANDOMIZED TRIAL

Unlike the above mentioned trials the EORTC trial failed to demonstrate any survival benefit in patients undergoing perioperative chemotherapy. In this trial patients with locally advanced disease was recruited and they were randomized in to surgery alone and surgery plus chemotherapy group. They used Cisplatin and five-fluorouracil as chemotherapeutic agents. The group which received perioperative chemotherapy had more post operative complications. At median follow up of 4.4 years the patients had no survival advantage.(40)

This trial showed a significantly increased R0 resection rate but failed to demonstrate a survival benefit. Possible explanations are low statistical power ( the study stopped due to poor accrual), a high rate of proximal gastric cancer including oesophageal adenocarcinomas and/or a better outcome than expected after radical surgery alone due to the high quality of surgery with extensive lymphadenectomy.(40)

## SURGERIES FOR GASTRIC CANCER

Surgery has remained the mainstay of treatment in carcinoma stomach and in essence is the only possible curative treatment in this disease. Therefore surgical resection should aim at complete removal of all macroscopically visible disease and direct at getting histological disease free margins. This result is reached in 45% of gastric cancers studied in population-based series and up to 55–60% of cases in high volume centers for gastrectomies. The type of operation conducted depends on the site, the T- stage of the disease and the extent of the lymph nodal involvement.(13)

### TOTAL GASTRECTOMY

Total gastrectomy is the removal of whole of the stomach for lesions in the upper and middle third of the stomach. Here, the stomach is resected en bloc including the entire greater omentum and lesser omentum. Adequate lymph node clearance is done. The gastrointestinal continuity is reconstructed by oesophagojejunostomy.

### SUBTOTAL GASTRECTOMY

This resection is done for distally placed tumors of the stomach where proximal stomach is preserved and the rest of the tumor is resected with 5 cm proximal clearance. The gastrointestinal continuity is reconstructed by gastrojejunostomy.

### PALLIATIVE SURGERY

In patients who have an advanced obstructing distal tumor or a bleeding tumor, palliative surgery is appropriate. Palliative surgery would include palliative gastrectomy which removes

the tumor and reconstructs the gastrointestinal tracts. The non surgical method of palliation of an obstructing tumor is by endoscopic stenting.

LYMPHADENECTOMY

D1 LYMPHADENECTOMY – involves removal of N1 nodes – stations 1 to 7.

This lymphadenectomy is done when nodes are N0.It is a removal of nodes along with lesser curve, greater curve and pylorus.

D2 LYMPHADENCTOMY involves removal of D2 nodes – D1 + stations 8 to 12.

This lymphadenectomy is done for N1 stage of the disease. Here nodal stations 1 to 11 are removed. (41)

D3 LYMPHADENCTOMY more distal nodes (stations 13 to 16 are removed).

This is done when nodal stage is N2.The nodes removed are hepato-duodenal along the middle colic artery. Hence nodal stations 1 to 16 are removed.

R0 RESECTION

Here a complete resection is done with no microscopic residual tumor.

R1 RESECTION

Here a complete resection is done with no macroscopic residual tumor. Yet the margins are positive for tumor tissue microscopically.

R2 RESECTION

Gross tumor is left behind at the end of resection. This resection at the most is only palliative.

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# MATERIALS AND METHODS

## STUDY SETTING:

Christian Medical College, Vellore is a 2200 bedded, tertiary care, multi-specialty teaching hospital in South India.

## STUDY DESIGN

This is a prospective study done among patients diagnosed with carcinoma stomach in the General Surgical Unit III of Christian Medical College and Hospital, Vellore from 1st September 2011 to 31st October 2013

**INCLUSION CRITERIA:**

Patients with histologically confirmed adenocarcinoma of stomach planned for surgical intervention based on preoperative staging investigations which should include computed tomography scan done within 8 weeks before surgery.

**EXCLUSION CRITERIA:**

1. Preoperative CT scan demonstrating distant metastasis.
2. General condition of the patient precluding any surgical intervention.
3. Previous surgeries precluding Laparoscopy.

**STUDY DURATION:**

1st September 2011 to 31st October 2013

**APPROVAL:**

This study was reviewed and cleared by the Institutional Review Board (IRB No: 7622) and the Ethics Committee of CMC Vellore.

Funding for the study was provided by the Fluid Research Grant.

## SAMPLE SIZE CALCULATION

Statistical method used to arrive at sample size was "Two Proportion – Hypothesis Testing – Large Proportion – Equal Allocation" method. The reference study used to arrive at the sample size was the one done by D Mahadevan et al, consecutive patients were studied and sensitivity of laparoscopy was compared to that of CT scan. Laparoscopy was found to more sensitive than CT in T3, T4 and M1 disease. (8)

Two Proportion - Hypothesis Testing - Large Proportion - Equal Allocation

Overall

Proportion in group I (CT-sensitivity) = 0.575

Proportion in group II (Laparoscopy-sensitivity) = 0.85

Risk difference = -0.275

Power (%) = 80

Alpha Error (%) = 5

Side = 2

Required sample size for each arm = 41

| Alpha Error (%) | Power (%) | Sample size |
|---|---|---|
| | 70 | 51 |
| 1 | 80 | 62 |
| | 90 | 78 |
| | | |
| | 70 | 33 |
| 5 | 80 | 41 |
| | 90 | 55 |
| | | |
| | 70 | 25 |
| 10 | 80 | 32 |
| | 90 | 44 |

Table 7: Sample size calculation

Similarly sample size with alpha error of 5% and power of 80 for M- stage, T2, T3, T4 were calculated to be 6, 58, 28 and 22 respectively. Hence for the study a sample size of 70 was considered taking into account attrition, dropouts during the study period.

Finally the results were calculated using Kappa statistics. Kappa coefficient is used as measure of inter observer agreement for qualitative items. The interpretation of Kappa values was made based on Altman (1991) criteria.(42)

Altman (1991) criteria

| Value of *K* | Strength of agreement |
|---|---|
| < 0.20 | Poor |
| 0.21 - 0.40 | Fair |
| 0.41 - 0.60 | Moderate |
| 0.61 - 0.80 | Good |
| 0.81 - 1.00 | Very good |

Table 8: Altman criteria for kappa statistics(42)

## METHODS

Patients with signs and symptoms suggestive of carcinoma stomach underwent endoscopy and lesion was biopsied. Those confirmed with adenocarcinoma on histopathology had a staging computed tomography. The CT findings were reported according to the standardized protocol. The time interval between the imaging and surgery was not more than 8 weeks.

A CT protocol has been designed for this study is given below.

CARCINOMA STOMACH CT PROTOCOL

PATIENT PREPARATION:

* 6 Hours fasting

* Water as contrast medium - 1000ml

* 400 ml to be administered immediately before examination

* Patient position:

Supine –for Gastric cardia or fundus lesion (based on endoscopic findings)

Prone - for distal to cardia or fundus (based on endoscopic findings)

CT scan was done using Philips Brilliance 6 slice CT scanner or Seimens Somatom Emotion 16 slice CT scanner. Both machines take the scan with 5mm cuts. Computed tomography was reported by single radiologist and recorded according to the following CT abdomen and pelvis reporting format.

Staging of disease was according to the criteria published by R. Hargunani et al, which was a modification of Ba-Ssalamah et al. According to this the staging by computed tomography was as follows

T STAGING

T0- No e/o alteration of gastric wall with preservation of normal fat plane

T1- Thickened mucosal layer with preserved low density stripe at the base of the lesion

T2 - Transmural enhancement with focal wall thickening

- Loss of layered structure
- Smooth outer border of the thickened gastric wall
- Clear fat planes around the lesion

T3 - Irregular outer border of the thickened gastric wall and / or a blurred fat plane around the lesion

T4 - Obliteration of fat plane between the gastric lesion and adjacent organs or infiltration of other organs

NODAL STAGING: Metastatic involvement of the nodes were based on following findings

Perigastric nodes - > 6mm

Extraperigastric nodes - > 8 mm

Round shape, longitudinal-transverse ratio - <1.5

Fatty hilum that is eccentric / missing

Marked heterogeneous enhancement

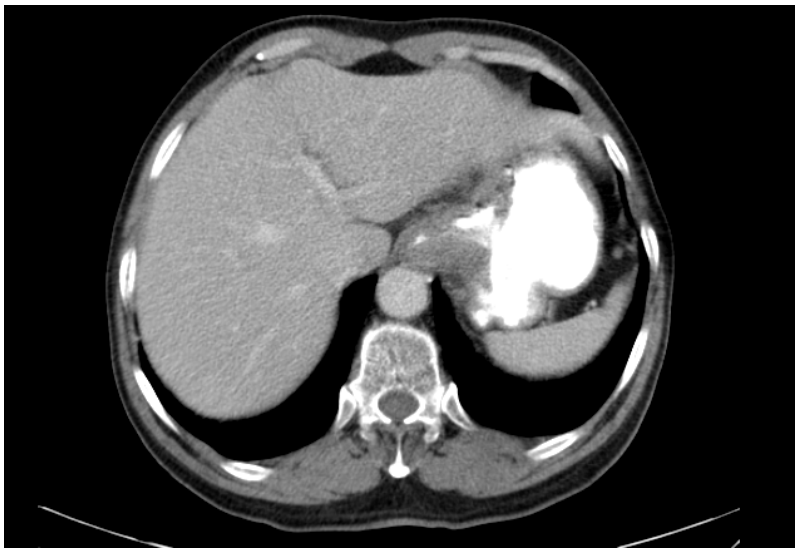

Figure 3: T3 lesion

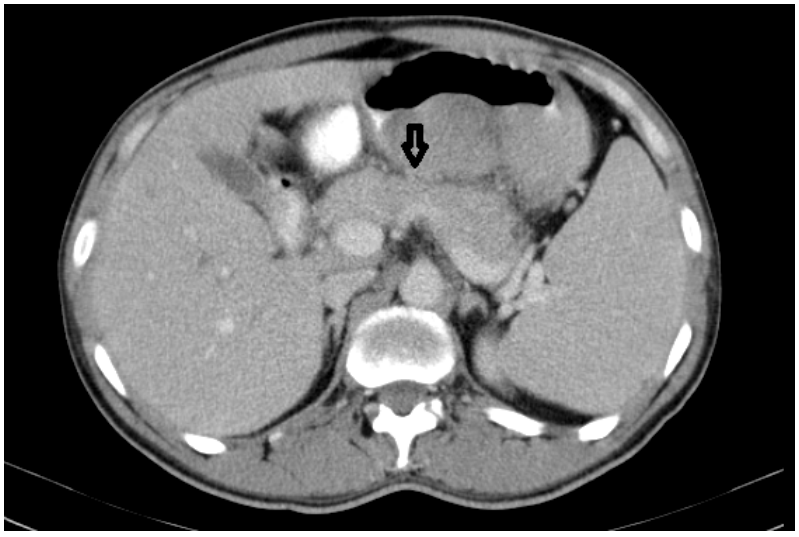

Figure 4: T4 lesion

**STAGING LAPAROSCOPY**

Those included in the study had a detailed plan of management made with inputs from the multidisciplinary team. These patients underwent preoperative evaluation for gastrectomy and pre anesthetic check up. Those deemed fit for anesthesia and major resection underwent staging laparoscopy under general anesthesia in the same sitting as the main surgery. Patients were placed in in supine position preoperative antibiotics were given at the time of induction. Nasogastric tube placed and urinary catheter was inserted under antibiotic cover. For the laparoscopy one 10mm supraumblical and two 5mm ports was used. Once the pneumoperitoneum is created with insufflation of carbon dioxide a 30 degree laparoscope was used to visualize the intraperitoneal contents. A suction device was introduced through one of the 5mm ports and ascitic fluid was suctioned for cytology.

7. Lesser sac ( lesser sac was entered only if there was no evidence of tumor deposits anteriorly )

Lesions on the peritoneum and liver surface were not routinely biopsied. Only when there was a doubt regarding the metastatic disease, a frozen section was performed. Metastatic lesions were classified into P1, P2, P3 and an on-table decision was made regarding the resection of the tumor. This was according to the flow chart given below:

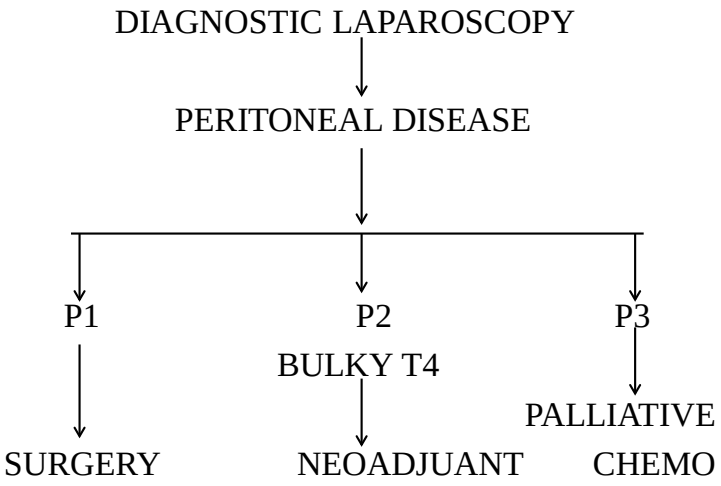


Figure 5: Peritonea disease treatment protocol

P1, P2, P3 are defined according to the recommendations of Japanese Research Society for Gastric Cancer.

P1 lesion: few metastases in adjacent peritoneum(9)

Figure 6: P1 lesion

P2 lesion: Few metastases to distant peritoneum(9)

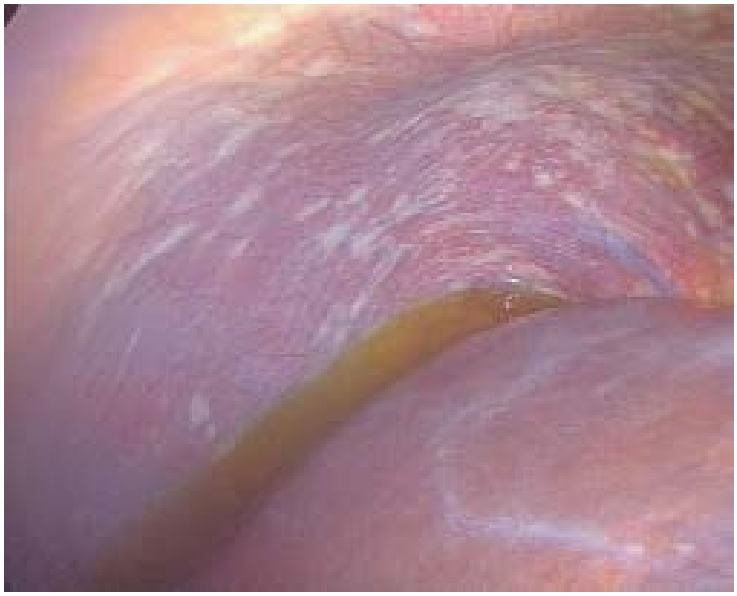

Figure 7: P2 lesion

P3 lesion: numerous metastases in distant peritoneum(9)

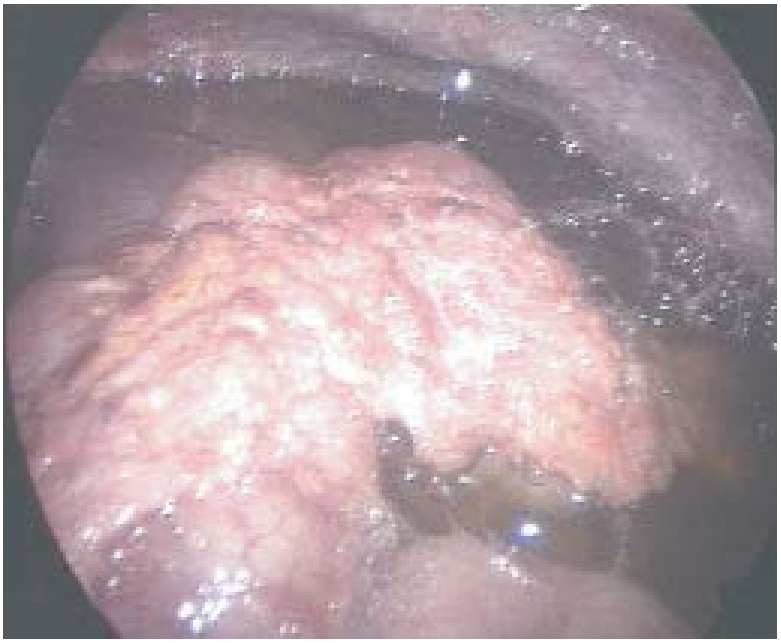

Figure 8**:** P3 lesion

If deemed necessary to confirm the diagnosis of metastasis biopsies were taken from the lesions.

The definition of variables T and M was according to the 7$^{th}$ edition of UICC Guidelines for staging of carcinoma stomach.

**PERITONEAL FLUID FOR CYTOLOGY**

Ascitic fluid was collected at the time of laparoscopy using suction device. Ascitic fluid was sent for cytology on the same day in specially provided 50ml bottle containing anticoagulant. The fluid was transferred into a Cytospin (Shandon) which centrifuges at 800rpm for 5 minutes. The slides made were treated with Cornoy's fixative for 5 minutes or in case of heavily blood stained slide for 15 minutes. The slide was treated with Isopropanol 95% and stained with Pap stain. All slides will be looked at and reported by the cytologist.

Clinical research form was used in entering all clinical data and relevant operative and post operative data. Histopathological staging of the disease was also entered.

Histopathology

Surgical specimen sent for histopathological examination was initially identified by the name and hospital number. Each specimen was given a barcode. Specimen was then sent for grossing. Gross study of the specimen was done by a pathologist. The specimen was then cut and placed in white or green colored cassettes. This was then treated with 10% formalin. Cassettes were then placed in an automatic processor (Lieca). The specimen passes through 70, 80, 90, 95% of alcohol and three containers of absolute alcohol and through three containers of toluene and finally through two buckets of paraffin. After 12 hours in the processor and embedding, the blocks were cut using a rotatory microtome which would yield 3 microns to 5 micron size specimen which was then stained with routine Haematoxylin and Eosin stains and study under microscope.

## RESULTS

### DEMOGRAPHICS

SEX DISTRIBUTION

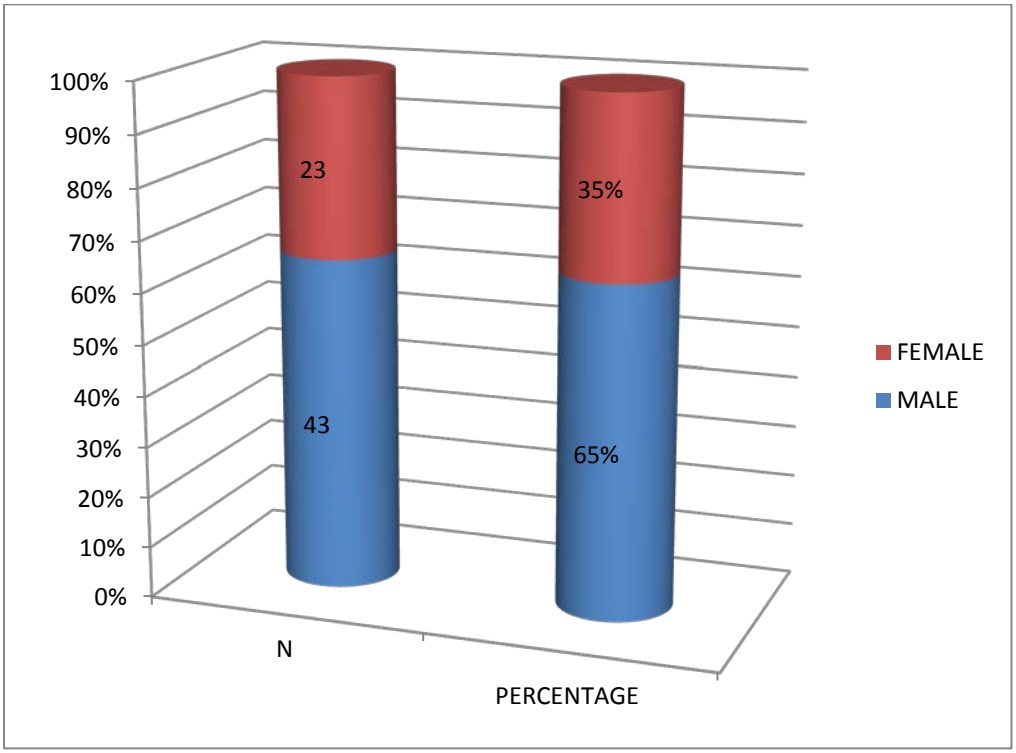


Figure 9: Sex distribution

There was male preponderance in our study with 65% of study population being males.

AGE DISTRIBUTION

| VARIABLE | MINIMUM | MAXIMUM | MEAN |
|---|---|---|---|
| AGE | 19 | 77 | 53 |

Table 9: Age distribution

Patients in their fifth decade were common in our study. Youngest patient was 19 years and oldest 77 years of age

TYPE OF HISTOLOGY

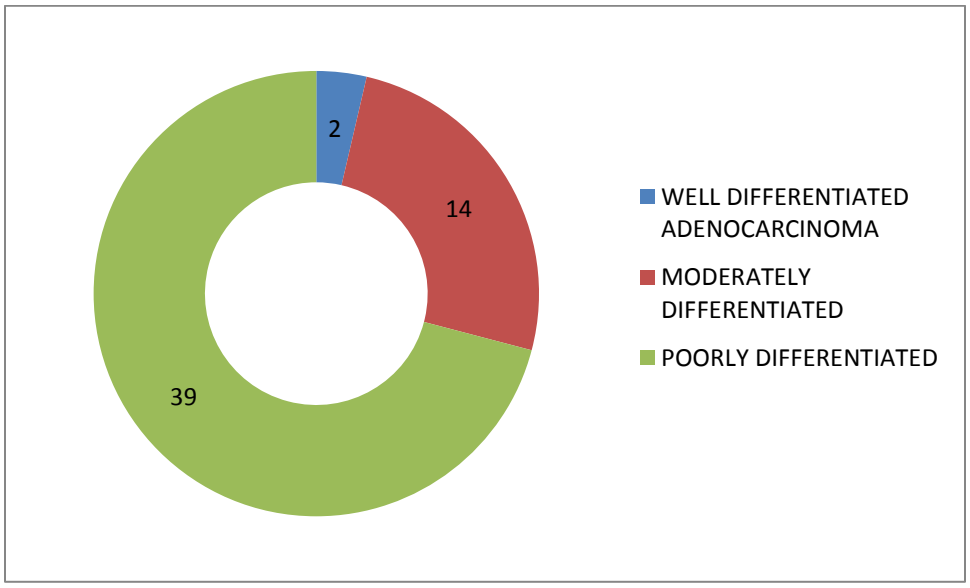


Figure 10: Type of histology

Poorly differentiated adenocarcinoma constituted the majority of histological types in this study population making up 70%.

PERITONEAL DISEASE DETECTED

PERITONEAL DISEASE ON COMPUTED TOMOGRAPHY Vs STAGING LAPAROSCOPY

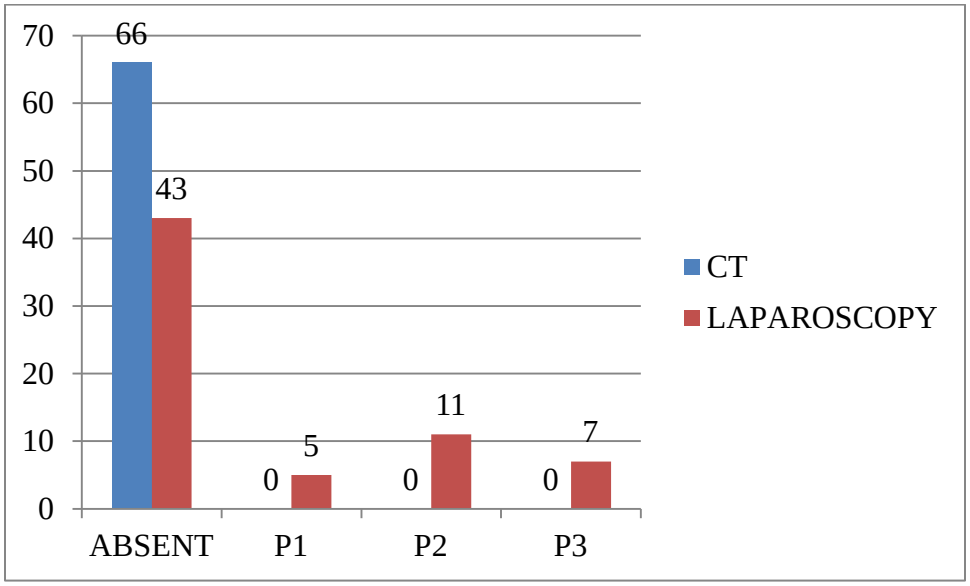


Figure 11: Peritoneal disease on CT Vs laparoscopy

CT – computed tomography

P1, P2, P3 – peritoneal metastases as described by Japanese classification

Of the 66 patients included in the study computed tomography did not pick up any peritoneal disease while staging laparoscopy detected 23 patients with peritoneal metastases. Of the 23 peritoneal metastases majority was P2 disease.

PERITONEAL DISEASE SPECIFIC TREATMENT DONE

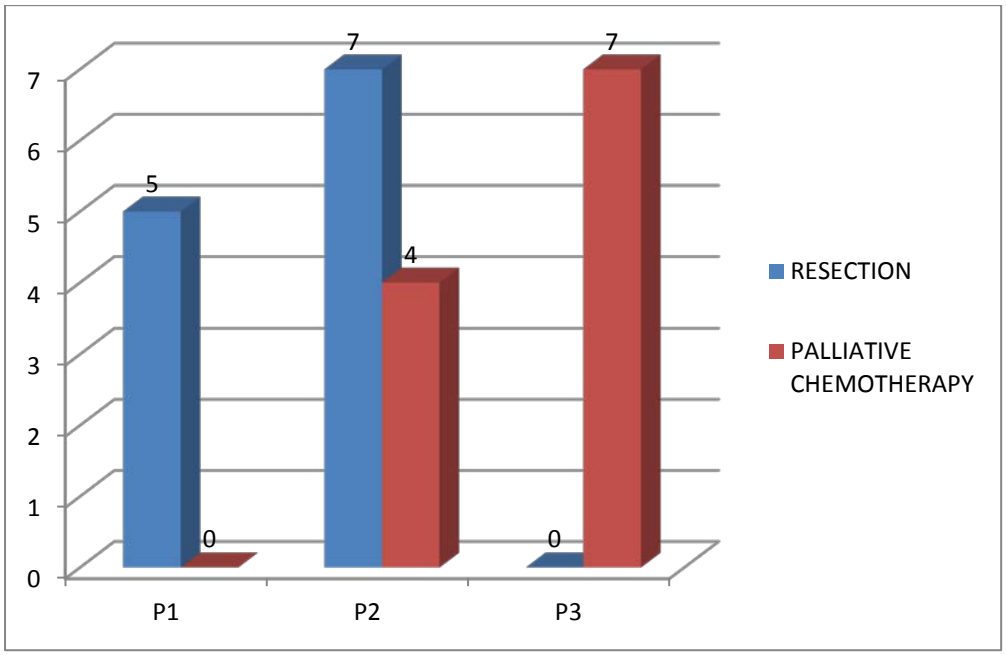


Figure 12: Peritoneal disease specific treatment instituted

All 5 patients with P1 disease, the laparoscopy was continued with a palliative gastric resection. Seven out 13 patients with P2 disease underwent palliative resection and in 4 patients with P2 disease, resection was abandoned and they underwent palliative chemotherapy. All seven patients who had P3 disease underwent palliative chemotherapy and had no resection.

ASCITIS AND LIVER METASTASES DETECTED

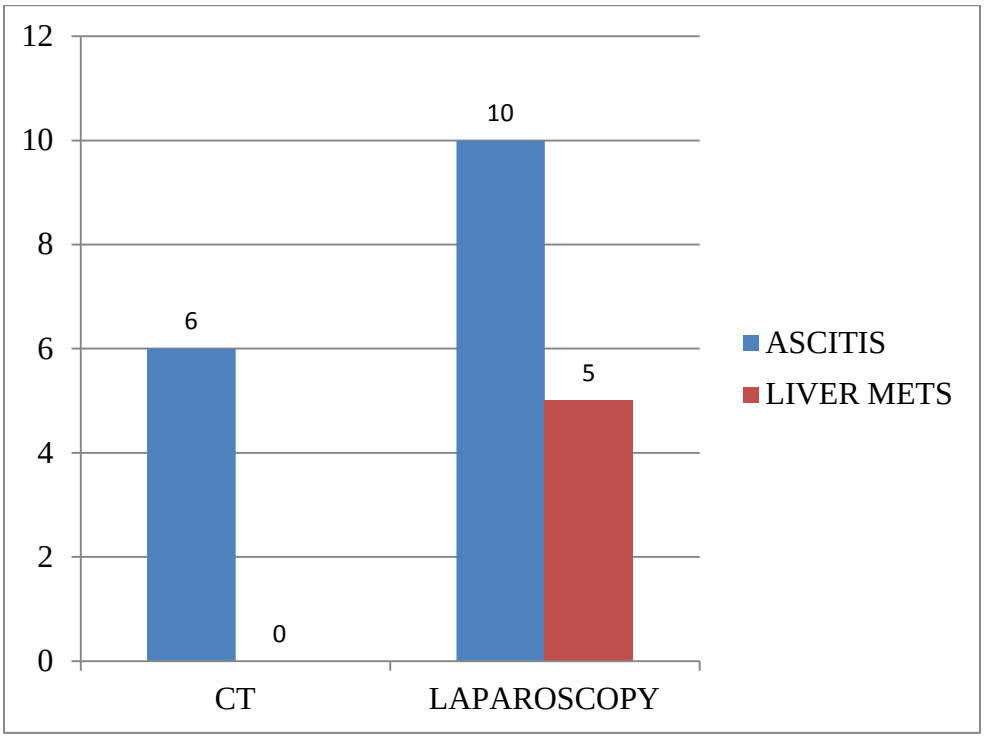


Figure 13: Comparison of ascitis and liver metastases detected on CT and laparoscopy

CT- computed tomography

Liver mets- liver metastases

Computed tomography detected 6 patients with ascites and none with liver metastases. On the contrary laparoscopy detected 10 patients with ascites and 5 with liver surface metastases.

CHANGE IN PLAN MADE AFTER STAGING LAPAROSCOPY

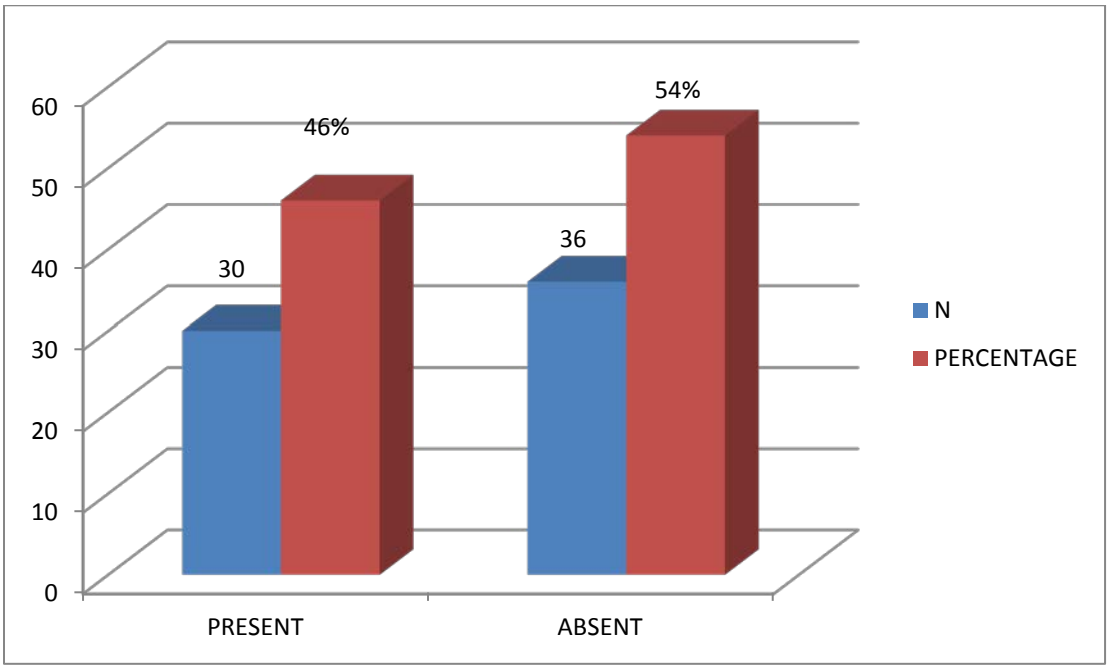


Figure 14: Change in plan according to laparoscopic findings

Based on staging laparoscopy a change in original plan was made in 46% of the study population. The original plan was executed in rest of the study population. This includes

1. Laparotomy avoided
2. Lymphadenectomy plan revised
3. Resection plan revised (curative to palliative or palliative to curative)

LAPAROTOMY AVOIDED

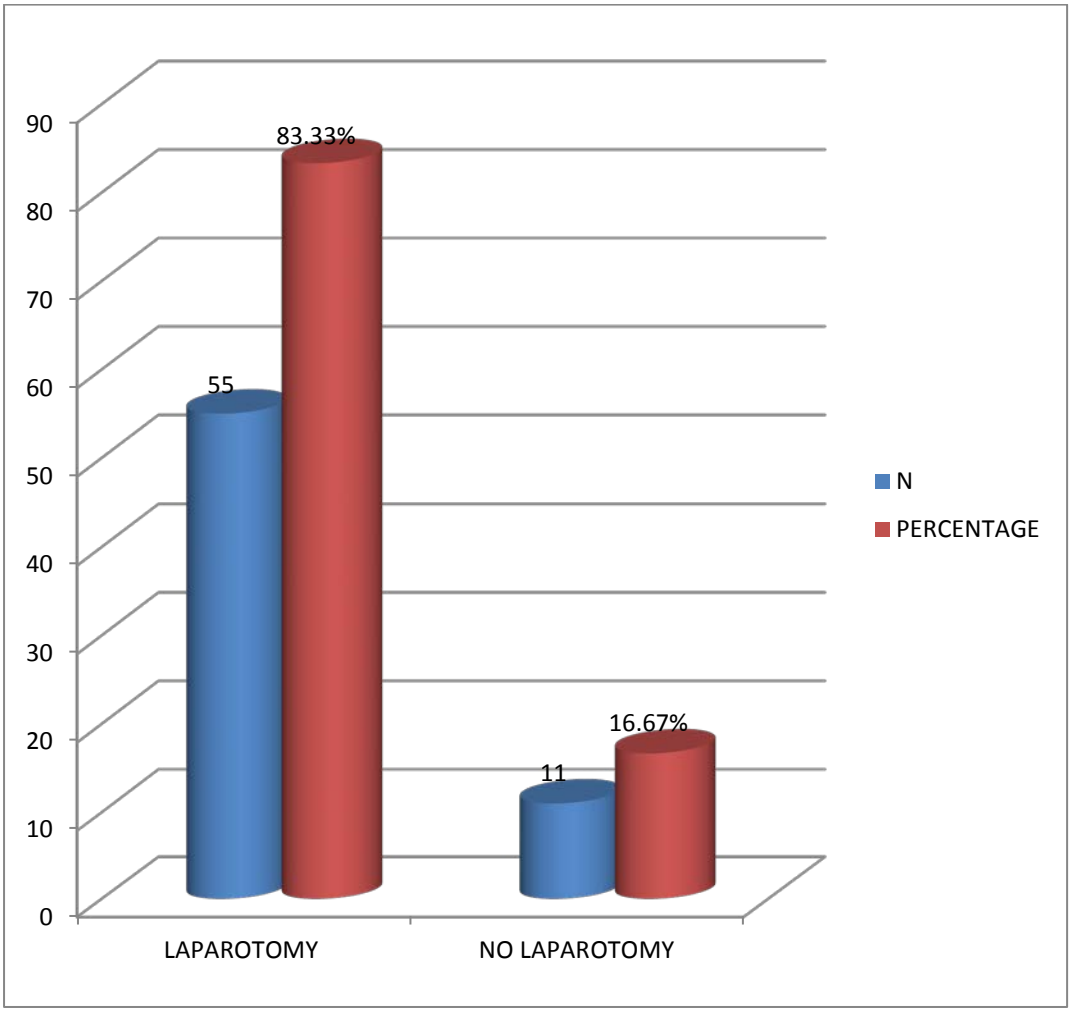


Figure 15: Laparotomy avoided

Based on the staging laparoscopic findings, unnecessary laparotomy was avoided in 16.67% of the study population.

RESECTION PLAN REVISED

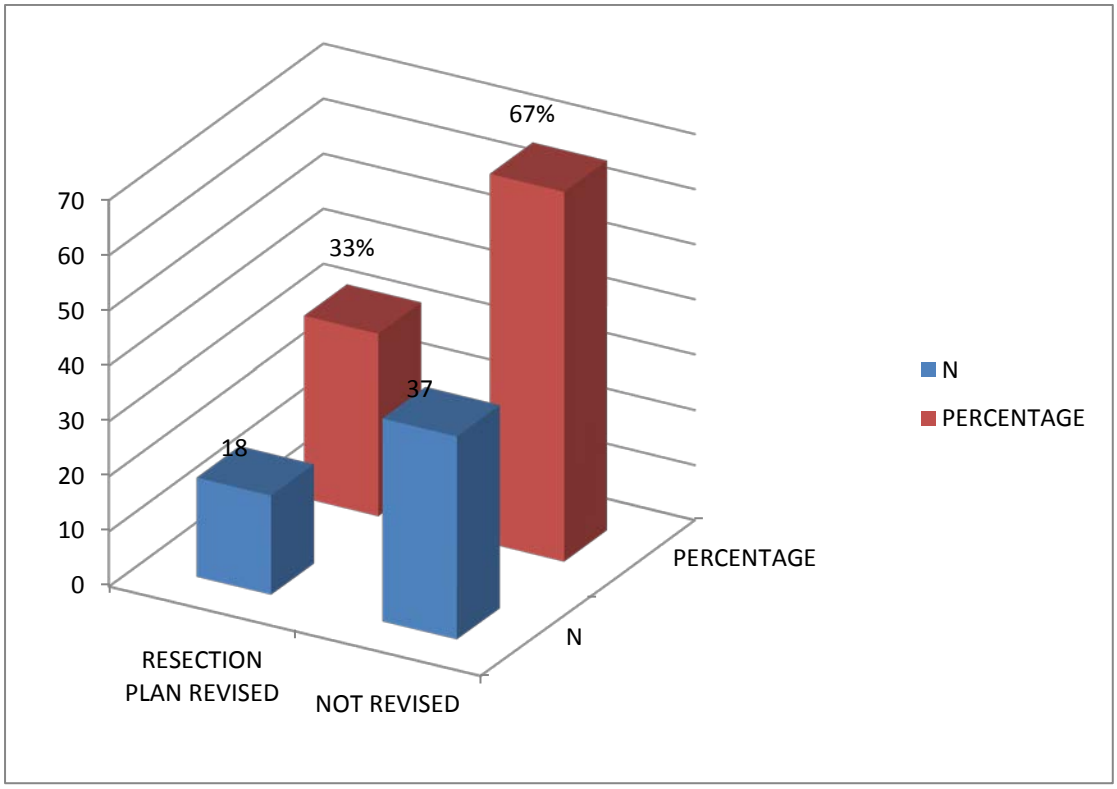


Figure 16: Resection plan revised

18 patients in the study had revision in original plan made for resection. The change in plan was from curative resection to palliative resection. This made up 33% of the study population.

LYMPHADENECTOMY PLAN REVISED

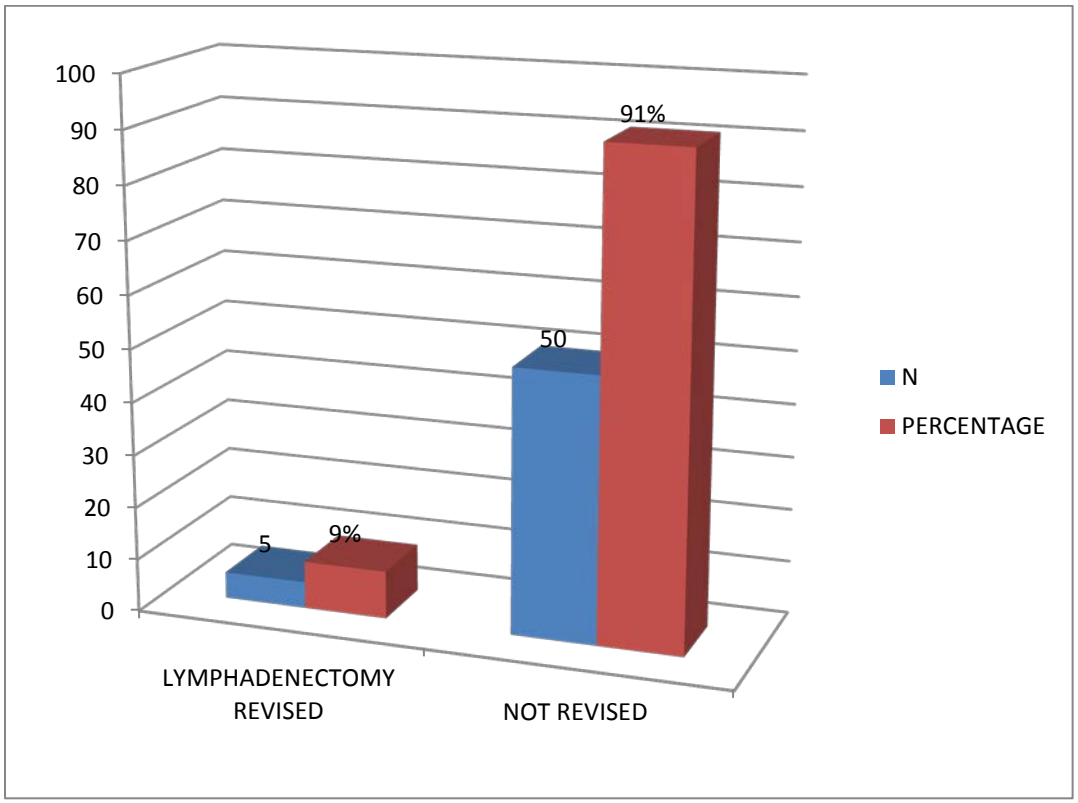


Figure 17: Lymphadenectomy plan revised

Lymphadenectomy plan was revised in 9 percentage of the study population in whom any form of resection was done. That is in these patients, the original plan was to perform a D2 gastrectomy. However in view of the peritoneal disease found, a lesser lymphadenectomy was performed.

OPERATION PERFORMED

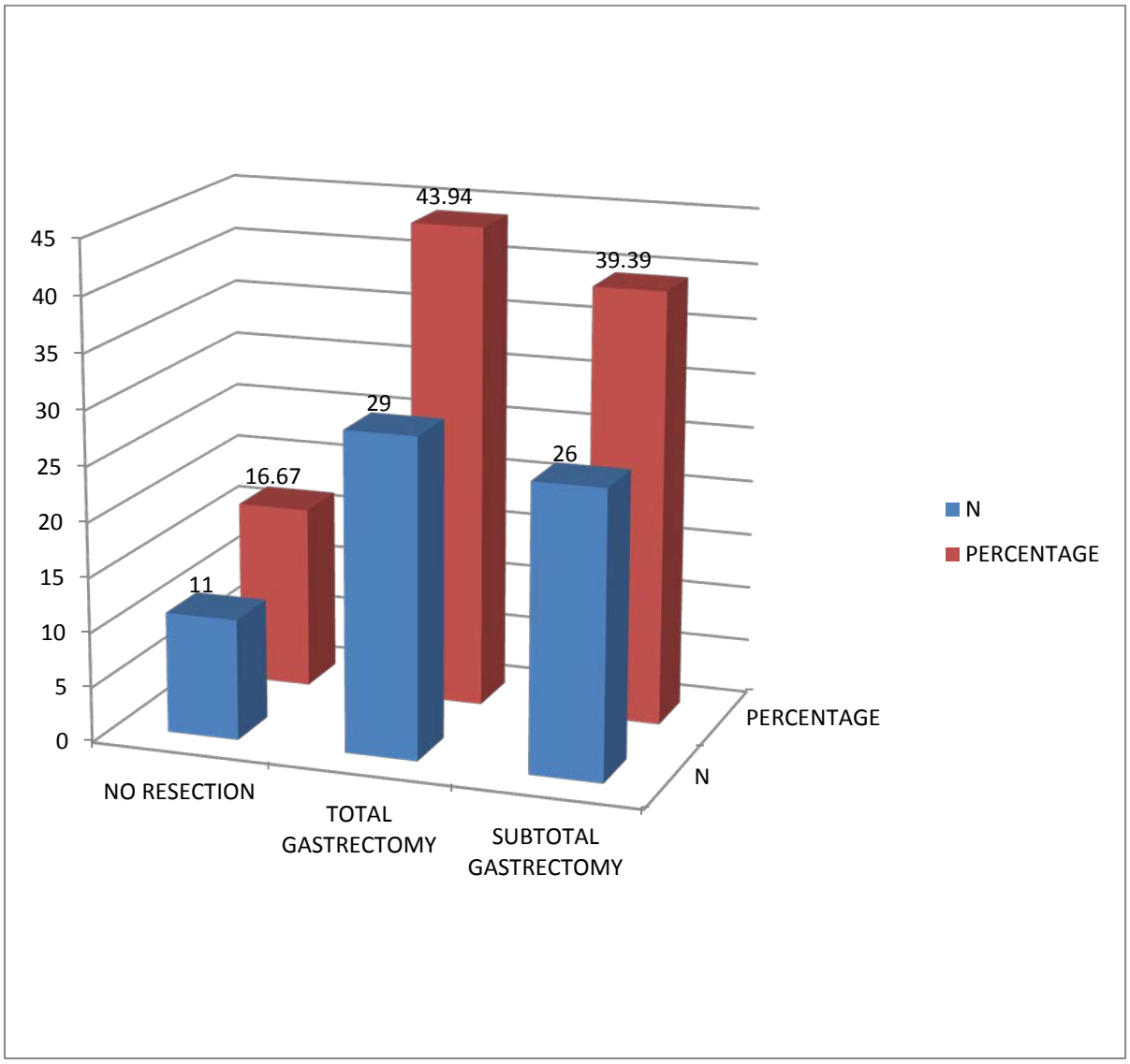


Figure 18:Operations performed

Major surgical resection was avoided in 16.67%. 44% of resectable tumors underwent total gastrectomy while rest had subtotal gastrectomy.

AGREEMENT OF CT AND LAPAROSCOPY WITH HISTOPATHOLOGY FOR T- STAGE OF THE TUMOR

| | CT | LAPAROSCOPY |
|---|---|---|
| k | 0.194 | 0.342 |
| p | 0.0133 | 0.0004 |

Table 10: Agreement of ct and laparoscopy with histopathology for t- stage of the tumor

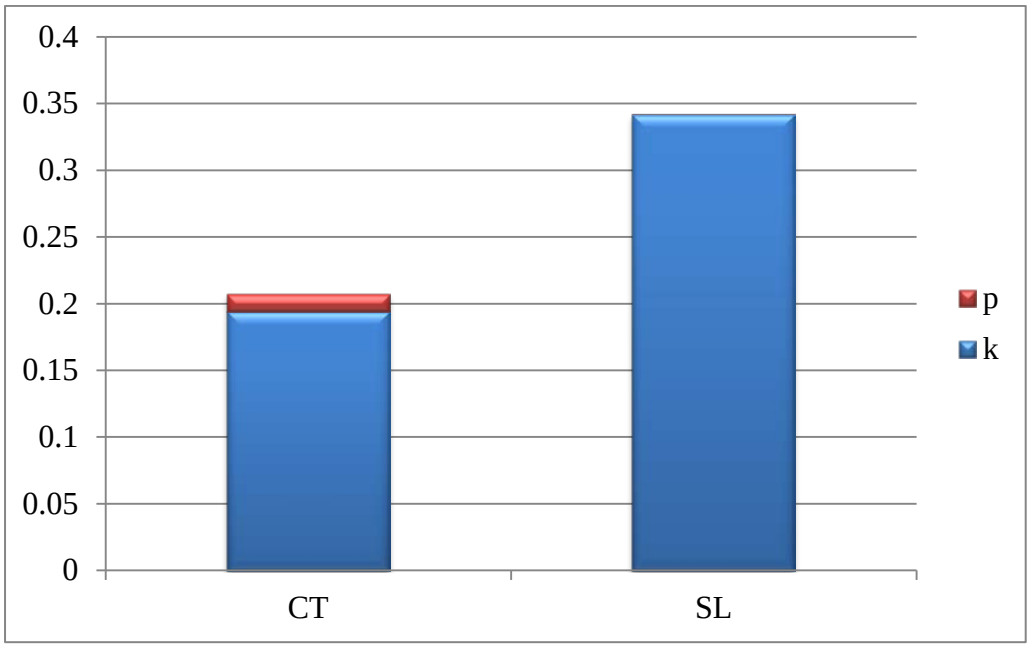


Figure 19: Agreement of ct and laparoscopy with histopathology for t- stage of the tumor

CT- computed tomography

SL- staging laparoscopy

p- P value

k- Kappa value

The kappa value for computed tomography for T- stage was 0.194. This according to the Altman criteria is poor agreement with gold standard. However this is not statistically significant because the p value above 0.05.

The kappa value of 0.342 for staging laparoscopy for T- stage shows fair agreement with gold standard and this is statistically significant.

AGREEMENT OF CT AND LAPAROSCOPIC FINDINGS WITH HISTOPATHOLOGY FOR SITE OF THE TUMOR

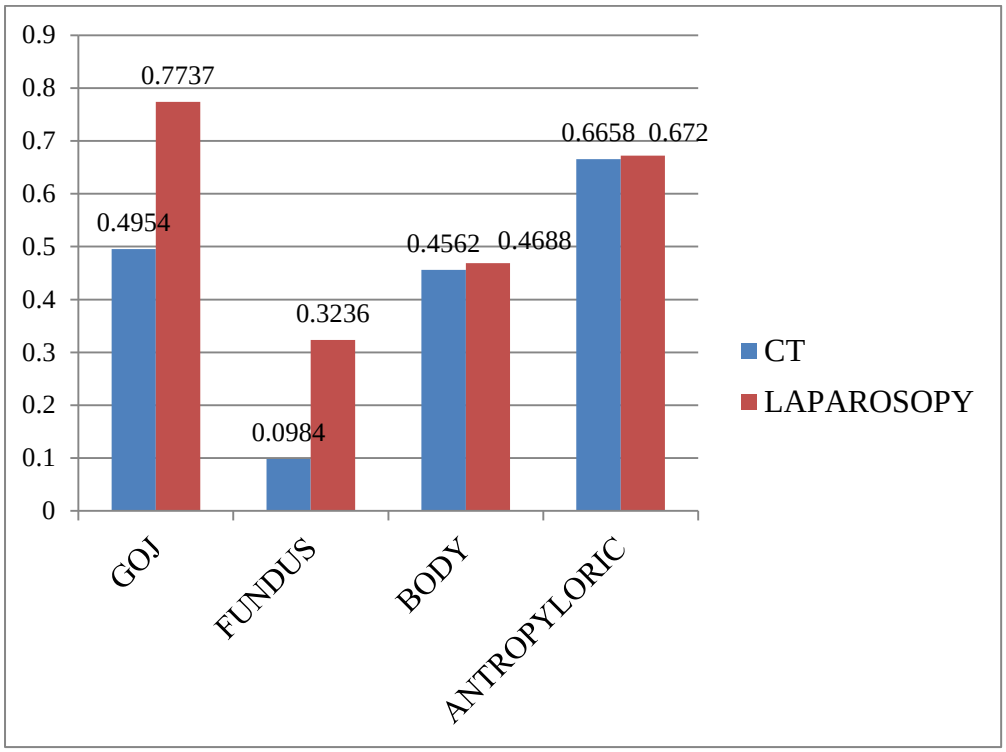


Figure 20: Kappa value for computed tomography and staging laparoscopy for tumor site

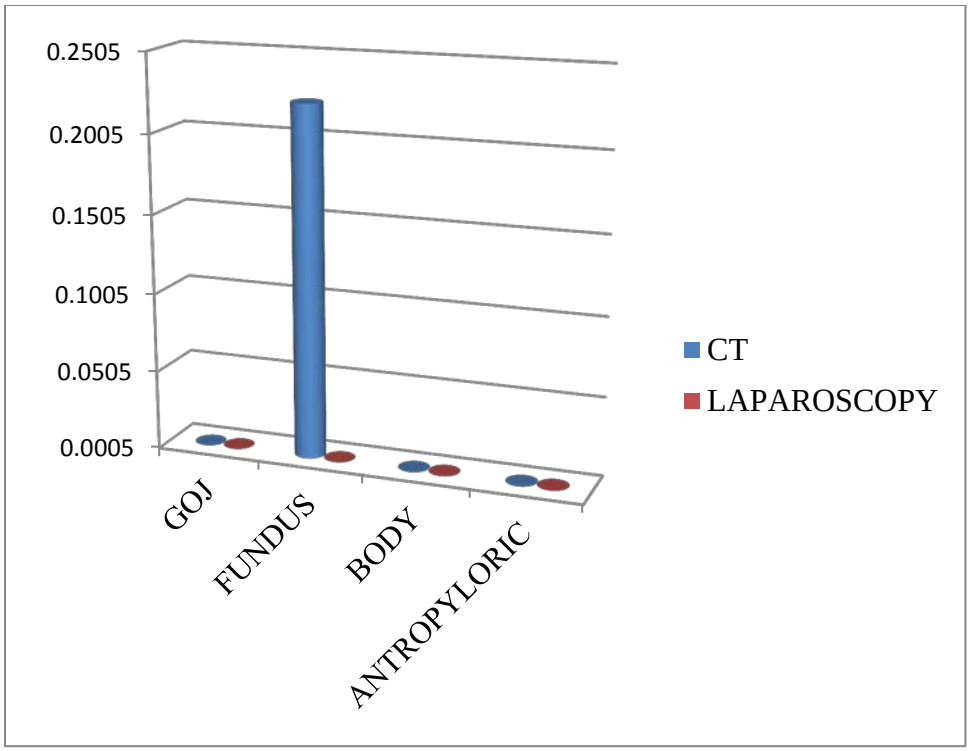


Figure 21: P value for the site of the tumor

CT- computed tomography

For distal tumours, CT scan and laparoscopy are equally effective in assessing T staging. However, in proximal tumours, staging lap scores over CT scan.

PERITONEAL FLUID CYTOLOGY

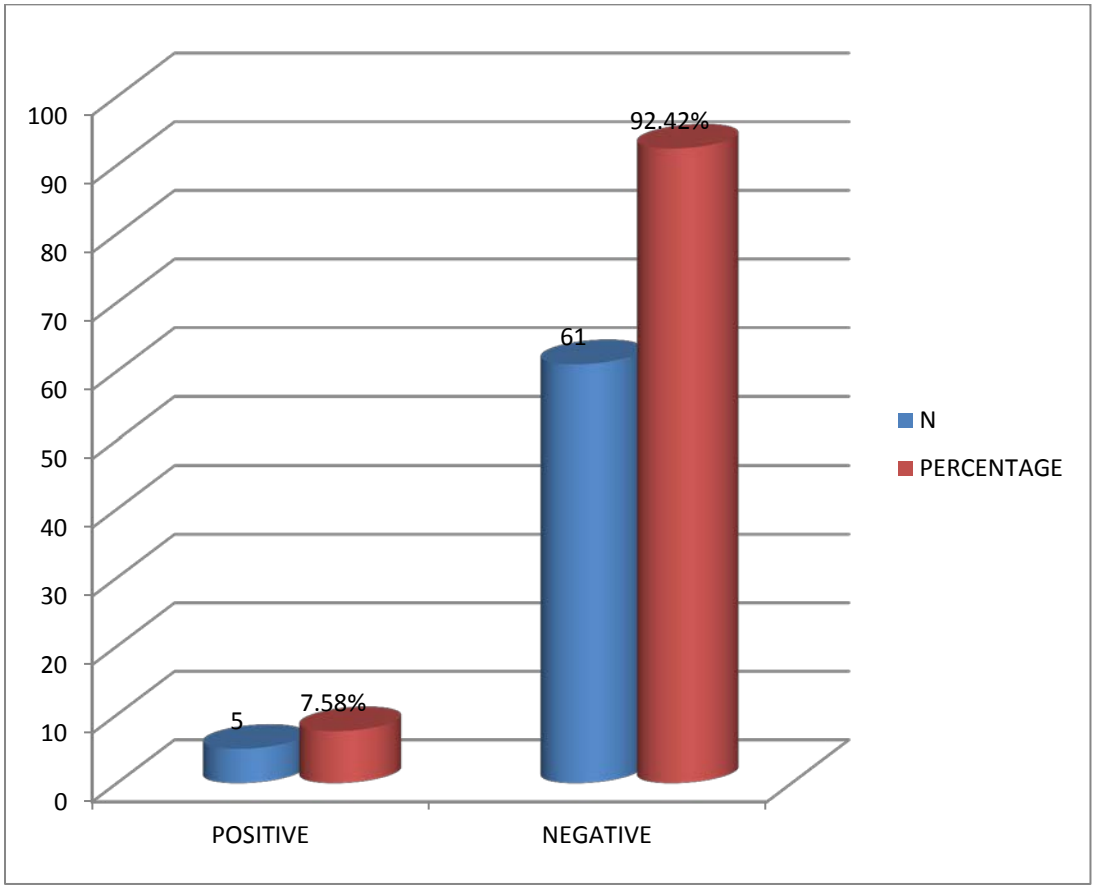


Figure 22: Peritoneal fluid cytology positivity rate

Peritoneal fluid positive rate was 7.58%

HISTOPATHOLOGICAL T- STAGE

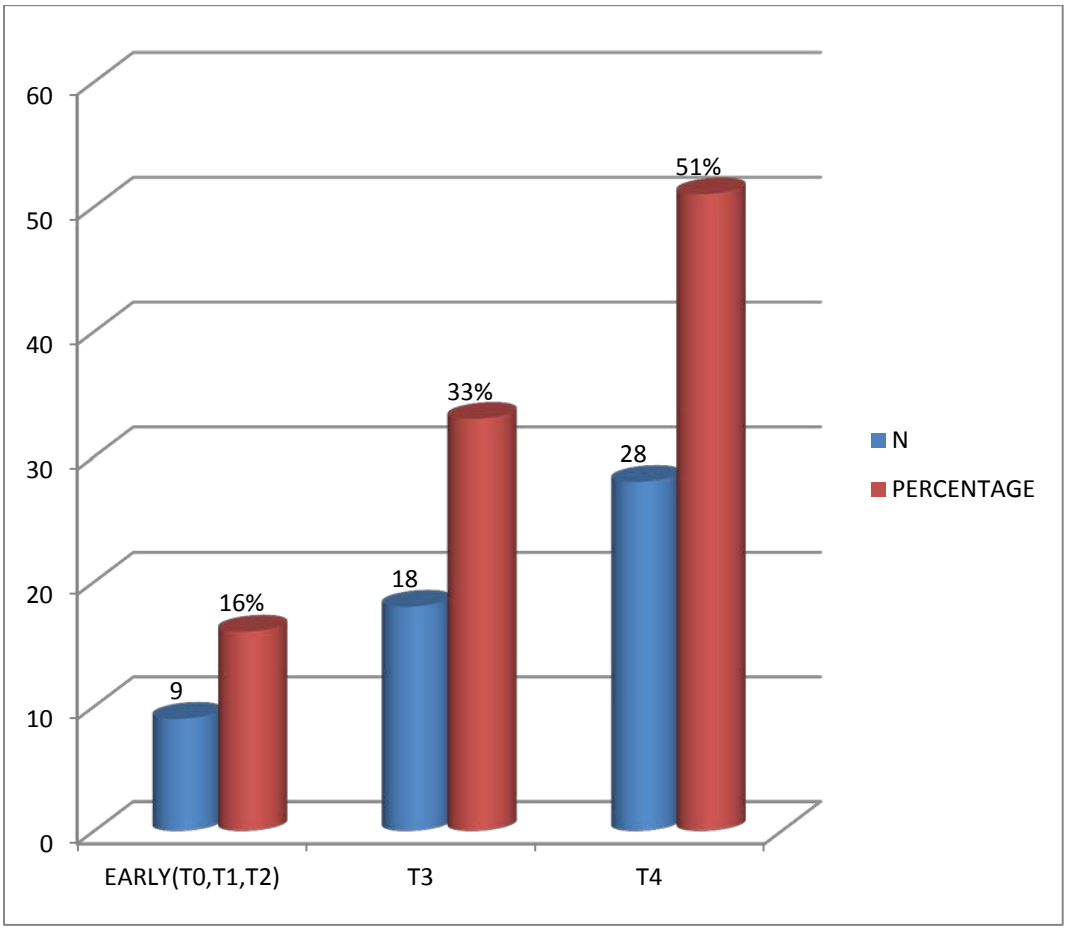


Figure 23: Final pathological T- stage

Majority of the tumors were T4 (51%) and it was followed by T3 disease (33%).

PERITONEAL DISEASE BREAK UP ACCORDING TO THE T- STAGES

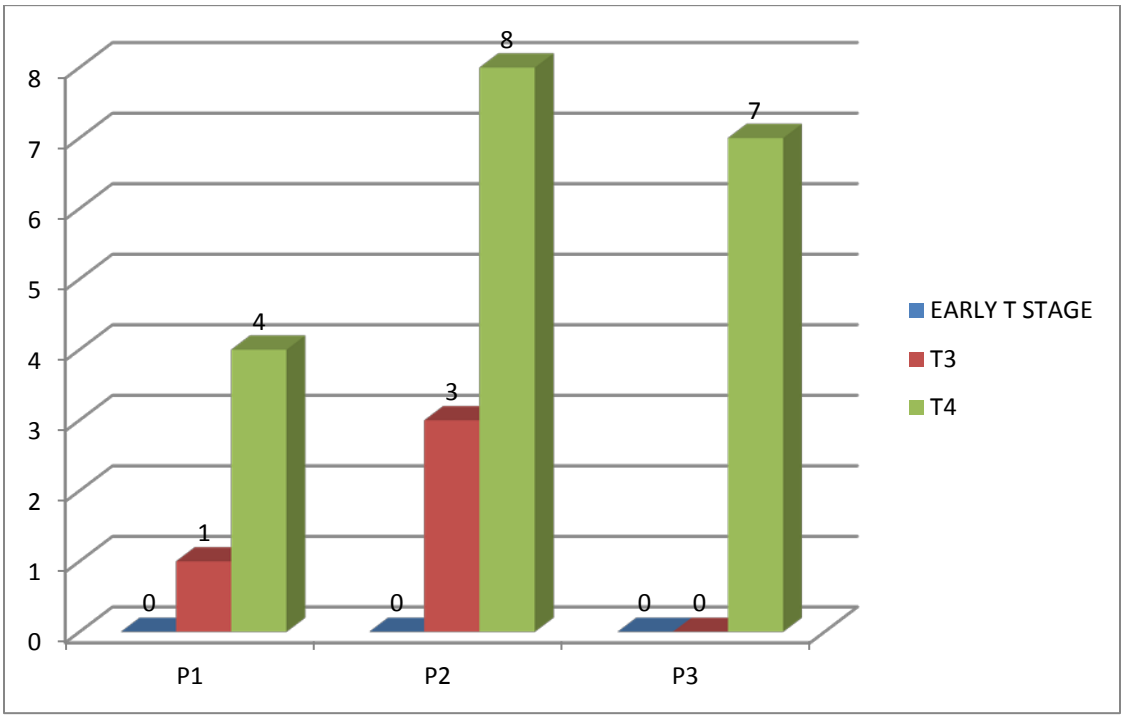


Figure 24: peritoneal disease according to T-stages

Peritoneal disease was found only in T3 and T4 disease. None of the patients with T1 or T2 disease had peritoneal disease. As expected, the majority of peritoneal disease was found in patients with T4 disease.

HISTOPATHOLOGICAL N- STAGE

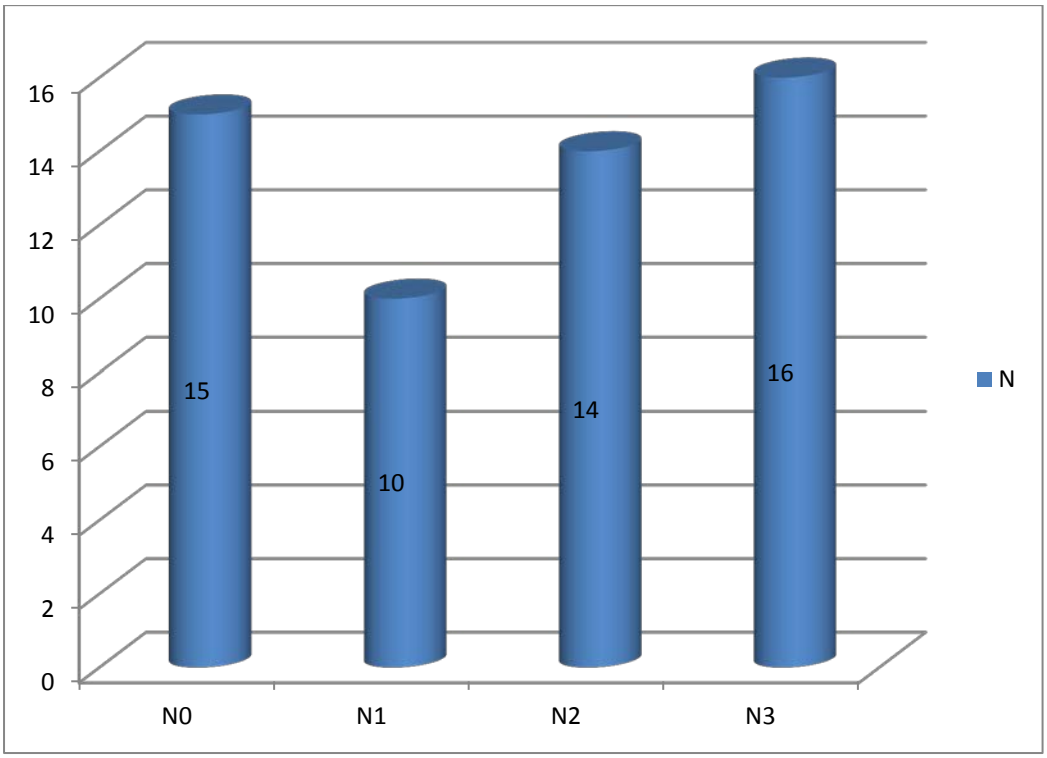


Figure 25: Final pathological N- stage

Majority of the patients had N3 or N0 disease.

DURATION OF LAPAROSCOPY

| VARIABLE | MEAN | MINIMUM | MAXIMUM |
|---|---|---|---|
| LAP DURATION | 20.29 | 10 | 60 |

Table 11: Duration of staging laparoscopy in minutes

The staging laparoscopy was performed just prior to the planned resectional surgery. Therefore this may not be an accurate representation of the actual time needed for the staging procedure alone.

Maximum time taken for performing staging laparoscopy was 60 minutes. The time taken was more when a frozen section biopsy was performed, in select patients. The average time taken for the staging laparoscopy procedure in this study was 20 minutes.

## DISCUSSION

Carcinoma stomach remains one of the commonest causes of cancer related deaths in India. In the light of ever changing technology in diagnostics, newer insights into chemotherapeutic agents, surgical skills, there needs to be a relook at the tools we employ to stage the disease. We studied the use of laparoscopy as a staging tool in carcinoma stomach. It was compared with computed tomography. 74 patients who were diagnosed with carcinoma stomach by endoscopy and biopsy were analysed. All patients had computed tomography as the preliminary staging investigation. Among the 74 patients, 8 who had a staging computed tomography at other centers were excluded from the study to bring uniformity in procedure and reporting of the scans. 66 patients were therefore included in the final analysis.

DEMOGRAPHICS

A male preponderance was seen, with 65% of the study cohort being males and 35% being females. The mean age of the study population was 53 years. The minimum age was 19 years and maximum age was 77 years. These demographic findings are in keeping with the literature. (14)

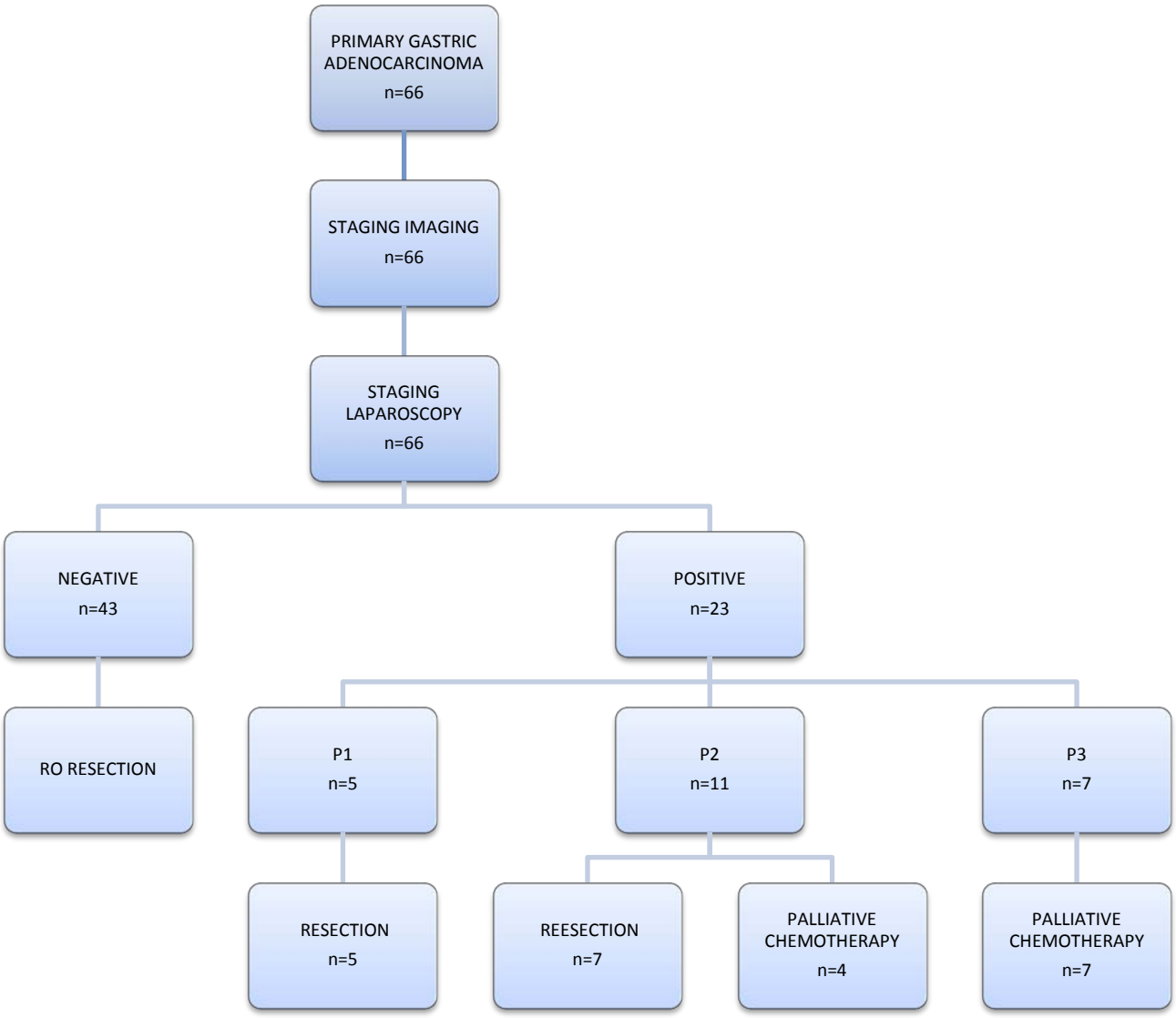


Figure 26: Prospective study comparing CT and Staging laparoscopy findings and assessing the impact on treatment plan.

SAFETY OF THE PROCEDURE

There is general agreement that staging laparoscopy is a safe procedure. It is well tolerated and the immediate complications are minimal with rate ranging from 0 to 3 percent. In this study patients who were deemed operable on computed tomography underwent staging laparoscopy. There were no major complications associated with the staging laparoscopy. (7)(9)

CONTRIBUTION OF LAPAROSCOPY IN CHANGE OF TREATMENT PLAN

There was a change in plan in 30 patients out of 66 patients recruited for the study. This constituted 46% of the study population. The original plan was executed in rest of the study population. Systematic review by Leake et al did show the use of staging laparoscopy altered treatment in 8.5%to 59.6% of cases in various studies.(43) The various changes in treatment plan included the following:

1. Laparotomy avoided
2. Lymphadenectomy revised
3. Resection plan revised

The most important finding of this study was that unnecessary laparotomy was avoided in 11 patients of the 66 patients recruited for the surgery. This was 15% of the study population. A systematic review by Leake et al of 21 articles published between January 1998 and December 2009 on the accuracy and indication of staging laparoscopy showed that the laparotomy was avoided in 8.5% to 43.8%.(43)

Lymphadenectomy revised was revised in 5 patients out 55 patients who underwent resection (9%). Similarly Resection plan was revised from either curative to palliative or palliative to curative in 18 patients (33%).

## ABILITY OF STAGING LAPAROSCOPY TO DETECT PERITONEAL DISEASE AND LIVER SURFACE METASTASES UNDETECTED ON COMPUTED TOMOGRAPHY

There are many studies which show that computed tomography can miss peritoneal and surface liver metastases. This study showed that laparoscopy could detect peritoneal disease and liver surface metastases which computed tomography could not detect. Peritoneal disease was classified into P1, P2 and P3 – peritoneal metastases as described by Japanese classification.(9) Of the 66 patients included in the study computed tomography did not pick up any peritoneal disease while laparoscopy staging laparoscopy detected 23 patients with peritoneal metastases. Five of these were P1 disease, 11 were P2 disease and 7 were P3 disease. Computed tomography detected 6 patients with ascites and none with liver metastases. On the contrary laparoscopy detected 10 patients with ascites and 5 with liver surface metastases.

Possik et al have shown that the sensitivity for peritoneal metastases for laparoscopy is 87% and for liver metastases is 87%. In a study conducted by Gretschel et al the sensitivity of laparoscopy for peritoneal disease was 85%. While that of computed tomography was 28%. He concluded that the aim of laparoscopic staging should involve detecting all patients with P3 disease as this group does not benefit from any surgical resection and on the contrary it will

add on to their morbidity. Patients with numerous peritoneal deposits who undergo laparotomy have higher postoperative morbidity (13–23 per cent) and mortality (10–26 per cent).(7)(9)

STAGING LAPAROSCOPY IN EARLY AND ADVANCED GASTRIC CANCER

It was noted in this study that all the patients who had peritoneal disease detected on staging laparoscopy had either T3 or T4 disease. This is in concordance with the current literature. So a staging laparoscopy may be safely avoided when the disease is limited to the mucosa and submucosa (T1). However when the disease involves the muscularis mucosa or beyond, (T2 or beyond), a staging laparoscopy forms an essential part of the staging and needs to be performed.

AGREEMENT OF LAPAROSCOPIC FINDINGS WITH THAT OF HISTOPATHOLOGICAL FINDINGS

In this study we looked at the ability of staging laparoscopy to detect the T stage of tumor. In 55 patients who underwent resection the findings of the computed tomography and laparoscopy were compared with the gold standard i.e. the histopathology. Statistical measure used here was the kappa statistics which looks into the agreement of the two tests with gold standard. The kappa value for computed tomography for T- stage was 0.194. This according to the Altman criteria is poor agreement with gold standard and is not statistically significant ($p > 0.05$). The kappa value of 0.342 for staging laparoscopy for T- stage shows fair agreement with gold standard and this was statistically significant.

When site specific agreement was looked at, both computed tomography and laparoscopy gives good agreement values for distal tumours. . However for the more proximal the tumors, laparoscopy identifies the site better than the CT scan. These findings are in agreement with systematic review by Leake P A et al, where the laparoscopic findings had moderate to substantial agreement with the final pathological findings when kappa statistics were used. There have been a few Indian studies in this regard. The recent one done by Kakroo et al found that the laparoscopy identifies the T-Stage of the disease with diagnostic accuracy of 81% with a sensitivity of 76% and specificity of 90%.

SIGNIFICANCE OF PERITONEAL FLUID POSITIVITY

Performing laparoscopy also helped in collecting peritoneal fluid for cytology. Peritoneal fluid was positive in 7.58% by using the routine papanicolaou staining. Those patients with positive peritoneal cytology are bound to harbor micro metastases on the peritoneum. They are at a higher risk in developing in disseminated peritoneal carcinomatosis. According to the recent NCCN guideline s these patients will be considered as metastatic disease In Japan peritoneal washings have become mandatory and part of the staging system. They have grouped these patients into CY1 disease and are staged as stage IV by the Japanese Classification of Gastric Carcinoma. Hence the Japanese do not offer gastrectomy with a curative intent in these patients.(44)

## TIMING OF LAPAROSCOPY

In the west, laparoscopic staging is done as a standalone procedure, prior to the gastric resection. However in this study, the staging laparoscopy was done just prior to the resectional operation, in the same sitting. This was planned, so as to overcome the logistic constraints of operating time availability and also to avoid the additional financial constraints to the patient.

Our study shows that the staging laparoscopy can be effectively performed during the same sitting as the resectional operation and therefore avoiding the need for the second anesthetic procedure.

## CONCLUSIONS

1. Laparoscopic staging adds additional staging information in the staging of carcinoma stomach.
2. Peritoneal disease and liver surface metastases are better detected by laparoscopy than computed tomography. The detection of these can avoid unwarranted resectional surgery.
3. The detection of T4 disease was better by staging laparoscopy, when compared to CT scan.
4. Laparoscopy was better than the CT scan in assessing the proximally located tumors of the stomach.
5. Peritoneal fluid cytology has a low detection rate when Papanicolaou stain is used. It did not add value to the laparoscopic staging due to its proximity to the resection.
6. Staging laparoscopy may be effectively performed in the same sitting as the primary operation, thereby avoiding the need for an additional procedure under general anesthesia.

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**ANNEXURE**

1

# CLINICAL RESEARCH FORM

## Staging Laparoscopy in Carcinoma Stomach

| | | | |
|---|---|---|---|
| **PATIENT NAME** | | | |
| Hospital No. | | Address | |
| Age | | | |
| Sex | | | |
| Email ID | | | |
| Telephone | | | |

| |
|---|
| **Initial investigation leading to diagnosis:** endoscopy / barium meal / other |
| **Date of diagnosis:** |

| | |
|---|---|
| **Barium meal: Y / N**<br><br>Date: _____<br><br>Findings: | **Endoscopy: Y / N**<br>Date: _____<br>Site of ulcer / tumour:<br>GOJ<br>Fundus: GC / LC<br>Body: GC / LC<br>Antrum: GC / LC<br><br>Histology: |

| | |
|---|---|
| **CT chest / Abdomen: Y/N**<br>Date: _____<br><br>Site of tumour:<br>Thickening of stomach: P / A<br>Loco regional spread: P / A<br>Ascites: P / A<br>Nodes: P / A | Liver mets: P / A<br>Lung mets: P / A<br>Peritoneal mets P/A |

| | |
|---|---|
| **PET Scan: Y/N**<br>Date: _____<br>Metastasis: Y/N<br>Location of mets: | **Endoscopic US: Y/N**<br>Date: _____<br>Staging:T<br>N<br>FNA node done: Y/N |

| | |
|---|---|
| **Pre op staging:**<br><br>**T____N____M____** | **MDTM**<br>**Date:** _____<br>**Plan:** |

## PART – B – Surgical

**Date of surgery:**
**Staging laparoscopy: Y/N**
**Findings:**
**Loco regional spread: P / A**
**Ascites: P / A**
**Nodes: P / A**
**Liver mets: P / A**
**Peritoneal mets P/A P1/ P2/P3**
**Cytology: +ve / -ve**
**Biopsies taken : Sites**

**Number**
**Surgery done:**

**Palliative / Curative:**
**Type of resection (SURG) – R0 / R1 / R2**
**Change in Plan**
**No change**
**Laparotomy avoided**

**Decision to attempt curative resection revised**
**Decision on lympadenectomy revised (D2 to D1,D1toD2)**
**Neoadjuant therapy**

**If palliative, Why? - Residual primary tumour**
**Residual nodes**
**Peritoneal disease**
**Liver mets**

**Histology:**

| | |
|---|---|
| Tumour site: C / F / B / A<br><br>Tumour type:<br><br>Tumour differentiation: Well diff<br>Moderately<br>Poorly<br><br>T: Tis / T1 / T2 / T3 / T4.<br><br>N:Nx / N0 / N1 / N2 / N3. | Proximal margin – involved / free of tumour<br><br>Distal margin: involved / free of tumour<br><br>Based on histology<br><br>Curative resection R0<br>Palliative resection R1<br>R2 |

## ANNEXURE 2

INFORMED CONSENT FORM

Study title: Laparoscopic staging of carcinoma of stomach and its impact on treatment plan.

Study Number:

Subject's Initial:

Date of Birth/ Age:

i. I confirm that I have read and understood the information sheet for the above mentioned study and have had the opportunity to ask questions to the investigator.
ii. I understand that my participation in the study is voluntary and that I am free to withdraw from the study at any point of time without giving any reason, without my medical care or legal rights being affected.
iii. I understand that my permission will not be required to look at my health records both in respect f the current study and any other further research that may be conducted in relation to it even if I withdraw from the study. I agree to this access. However I understand that my identity will not be revealed in any information released to third parties or published.
iv. I understand that my involvement in the study will include performing diagnostic Laparoscopy on me. The risks involved include 1) Bleeding0.3% 2)Wound site Infection 1.2% 3)Bowel injuries 0.2%
v. I understand that ascetic fluid cytology will be done and biopsies from suspicious lesions will be taken.
vi. I understand that photographic and or video graphic documentation of intraoperative findings will be done.

Herewith I give fully informed consent for the study.

Signature or thumb impression of the subject/legally acceptable representative

---

Date:

Place:

Signatory's Name:

Signature of the investigator: ----------

Date:

Investigator's Name :

Signature of the witness:----------

Date:

Name of the witness:

## ANNEXURE 3

**CT ABDOMEN AND PELVIS REPORTING FORMAT**

**Findings:**

**STOMACH :**

**Location and T staging of the mass**

**Loco-regional spread**

**See staging below**

**LIVER - comment on metastatic lesion**

**SPLEEN -**

**GB -**

**PANCREAS -**

**ADRENALS -**

**KIDNEYS -**

**BOWEL, MESENTERY, OMENTUM -**

**LYMPHADENOPATHY:**

**Mention nodal spread**

**--Perigastric**

**---Extra perigastric**

**a) greater omental -**

**b) lesser omental -**

**c) mesenteric -**

**d) diaphragmatic -**

**e) para-aortic -**

**f) para-iliac -**

**FLUID -Present / absent**

**BLADDER:**

**PROSTATE /UTERUS:**

**SEMINAL VESICLES/OVARIES**

**INGUINAL ORIFICES -**

**ABDOMINAL WALL -**

**BLOOD VESSELS -**

**VISUALISED LUNG BASES -**

**VISUALISED BONES -**

**IMPRESSION:**

**year old male / female with suspected carcinoma stomach, CECT abdomen shows:**

**Comment on:**

**1. Location**

**2. T staging**

**3. Loco regional spread**

**4. Nodal disease**

**5. Free fluid**

**6. Liver and peritoneal metastasis**

Office of the Addl. Vice Principal (Research)

Christian Medical College,
Vellore 632 002

Ref: Res/09/2011

December 13, 2011

Dr. Ashish Sam Samuel
PG Registrar
Department of Surgery
Christian Medical College
Vellore 632 002

Dear Dr. Samuel,

Sub: **FLUID Research grant project NEW PROPOSAL:**
Laparoscopic staging in carcinoma of the stomach and its impact on treatment plan
Dr. Ashish Sam Samuel, PG Registrar, Surgery, Dr. Inian Samarasam, Dr. Sam Varghese, General Surgery, Dr. Anu Eapen , Radiology, Dr. Anna Pulimood, Pathology, Dr. Dipti Masih, Pathology.

Ref: IRB Min. No. 7622 dated 3.10.2011

I enclose the following documents:-

1. Institutional Review Board approval
2. Agreement

Could you please sign the agreement and send it to Dr. Gagandeep Kang, Addl. Vice Principal (Research), so that the grant money can be released?

With best wishes,

Yours sincerely,

Dr. Alfred Job Daniel
Principal & Chairperson (Research Committee)
Institutional Review Board

| HOSPITAL N | AGE | SEX | ENDOSCOPY SITE | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | GOJ | | FUNDUS | | BODY | ANTR |
| | | | GC | LC | GC | LC | GC | |
| 447251F | 47 | M | 0 | 0 | 0 | 0 | 0 | 1 |
| 440326F | 63 | M | 0 | 0 | 0 | 0 | 1 | 1 |
| 385327F | 49 | M | 1 | 0 | 0 | 0 | 0 | 0 |
| 721760C | 64 | M | 1 | 0 | 0 | 1 | 1 | 1 |
| 371381F | 45 | M | 1 | 0 | 0 | 0 | 0 | 0 |
| 077339D | 60 | M | 0 | 0 | 0 | 0 | 0 | 1 |
| 071079F | 62 | M | 0 | 0 | 0 | 0 | 0 | 1 |
| 098268F | 45 | M | 0 | 0 | 0 | 0 | 1 | 0 |
| 919007D | 24 | F | 0 | 0 | 0 | 0 | 0 | 0 |
| 072749F | 37 | F | 0 | 0 | 0 | 0 | 0 | 1 |
| 049610F | 44 | F | 0 | 0 | 0 | 0 | 0 | 1 |
| 071969F | 56 | M | 0 | 0 | 0 | 0 | 1 | 0 |
| 131407F | 46 | M | 0 | 0 | 0 | 1 | 1 | 0 |
| 111674F | 50 | F | 1 | 1 | 0 | 1 | 0 | 0 |
| 080872F | 71 | F | 0 | 0 | 0 | 1 | 1 | 1 |
| 348642F | 58 | M | 0 | 0 | 0 | 0 | 0 | 1 |
| 259252F | 56 | M | 1 | 0 | 0 | 0 | 1 | 0 |
| 259614F | 58 | M | 0 | 0 | 0 | 0 | 1 | 0 |
| 265536F | 77 | M | 1 | 0 | 0 | 1 | 0 | 0 |
| 268714D | 56 | M | 0 | 0 | 0 | 1 | 1 | 0 |
| 274177F | 40 | F | 0 | 0 | 0 | 0 | 1 | 0 |

| RUM LC | SITE | | | | CT THICKENIN | LOCOREGIC | ASCITES | NODES |
|---|---|---|---|---|---|---|---|---|
| | GOJ | FUNDUS | BODY | ANTRUM | | | | |
| 1 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 |
| 1 | 0 | 0 | 0 | 1 | 1 | 0 | 1 | 1 |
| 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| 1 | 0 | 0 | 1 | 1 | 1 | 0 | 0 | 0 |
| 0 | 1 | 1 | 0 | 0 | 1 | 0 | 0 | 1 |
| 1 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 |
| 1 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 1 |
| 0 | 0 | 0 | 1 | 0 | 1 | 1 | 0 | 1 |
| 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 1 |
| 1 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 1 |
| 1 | 0 | 0 | 1 | 1 | 1 | 0 | 0 | 0 |
| 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 |
| 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 1 |
| 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 0 |
| 1 | 0 | 1 | 1 | 0 | 1 | 0 | 0 | 0 |
| 1 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 |
| 1 | 0 | 0 | 0 | 1 | 1 | 1 | 0 | 1 |
| 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 0 |
| 0 | 0 | 0 | 1 | 1 | 1 | 0 | 0 | 0 |
| 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 0 |

| LIVER METS | LUNGMETS | PERITONEA | T | | | | PREOP STAGIN | |
|---|---|---|---|---|---|---|---|---|
| | | | TIS | T1 | T2 | T3 | T4 | N0 | |
| 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 |
| 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 |
| 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 |
| 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 |
| 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 |
| 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 |
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 |
| 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 |
| 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 |
| 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 |
| 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 |
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 |
| 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 |
| 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 |
| 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 |
| 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 |

| NG | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | N | | | M | | SITE | | | |
| | N1 | N2 | N3 | M0 | M1 | GOJ | FUNDUS | BODY | ANTRUM |
| | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 |
| | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 1 |
| | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 0 |
| | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 |
| | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 0 | 0 |
| | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 |
| | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 |
| | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 |
| | 1 | 0 | 0 | 1 | 0 | 1 | 1 | 1 | 0 |
| | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 |
| | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 |
| | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 |
| | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 |
| | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 |
| | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 1 |
| | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 |
| | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |

| STAGING LAP | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| STAGE | | LOCOREGIC | ASCITES | NODES | LIVER METS | | PERITONEAL | |
| T3 | T4 | | | | | P1 | P2 | P3 |
| 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 0 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 1 |
| 0 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| 0 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 1 |
| 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 1 |
| 0 | 1 | 1 | 1 | 0 | 0 | 0 | 1 | 0 |
| 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 0 | 1 | 1 | 0 | 0 | 1 | 0 | 0 | 0 |
| 0 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| 0 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 0 | 1 | 0 | 1 | 1 | 1 | 0 | 1 | 0 |
| 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |

| CYTOLOGY | | BIOPSIES | SURGERY DONE | | | PALLIATIVE | CURATIVE | |
|---|---|---|---|---|---|---|---|---|
| POSITIVE | NEGATIVE | | TG | ST | NO RESECTION | | | R0 |
| 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 1 |
| 0 | 1 | 0 | 0 | 0 | 1 | 1 | 0 | 0 |
| 0 | 1 | 0 | 1 | 0 | 0 | 0 | 1 | 1 |
| 1 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 |
| 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 |
| 0 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 |
| 0 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 0 |
| 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 |
| 0 | 1 | 1 | 0 | 1 | 0 | 1 | 0 | 0 |
| 0 | 1 | 0 | 0 | 1 | 0 | 1 | 0 | 0 |
| 0 | 1 | 0 | 1 | 0 | 0 | 0 | 1 | 1 |
| 0 | 1 | 1 | 0 | 0 | 1 | 0 | 0 | 0 |
| 0 | 1 | 0 | 1 | 0 | 0 | 0 | 1 | 1 |
| 0 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 1 |
| 0 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 1 |
| 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 1 |
| 0 | 1 | 0 | 1 | 0 | 0 | 0 | 1 | 1 |
| 0 | 1 | 0 | 1 | 0 | 0 | 0 | 1 | 1 |
| 0 | 1 | 0 | 0 | 0 | 1 | 1 | 0 | 0 |
| 0 | 1 | 0 | 1 | 0 | 0 | 0 | 1 | 1 |

| RESECTION | | ANGE IN PLAN | | | | | PALLIAT | |
|---|---|---|---|---|---|---|---|---|
| R1 | R2 | NIL | LAPAROTO | RESECTION | LYMPH ADI | NT | RESIDUAL I | RESIDUAL N |
| 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| 0 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 1 |
| 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 1 |
| 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |

| IVE FOR PERITONEA | LIVER METS | SITE | | | | TUMOR TYPE | | | DIF |
|---|---|---|---|---|---|---|---|---|---|
| | | GOJ | FUNDUS | BODY | ANTRUM | ADENO | SQ | WELL | |
| 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | |
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | |
| 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| 1 | 0 | 0 | 0 | 1 | 1 | 1 | 0 | 0 | |
| 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | |
| 0 | 1 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | |
| 1 | 0 | 0 | 0 | 1 | 1 | 1 | 0 | 0 | |
| 1 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | |
| 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | |
| 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | |
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | |
| 0 | 0 | 0 | 0 | 1 | 1 | 1 | 0 | 0 | |
| 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | |
| 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | |
| 0 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | |
| 0 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | |
| 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| 0 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | |

| | | | HPE | | | | | |
|---|---|---|---|---|---|---|---|---|
| FERENTIATION | | T STAGE | | | | | N STAGE | |
| MOD | POORLY | TIS | T1 | T2 | T3 | T4 | N0 | N1 |
| 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 0 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 1 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 |
| 0 | 1 | 0 | 0 | 0 | 1 | 0 | 1 | 0 |
| 0 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 1 |
| 1 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| 0 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 1 |
| 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 |
| 0 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 0 | 1 | 0 | 0 | 0 | 0 | 1 | 1 | 0 |
| 0 | 1 | 0 | 0 | 0 | 1 | 0 | 1 | 0 |
| 0 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 1 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 |

| N2 | N3 | PROXIMAL | DISTAL | MA | CURATIVE R0 | R1 | PALLIATIVE R2 | | LAP DURATION |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 0 | 0 | 0 | | 1 | 0 | 0 | | 15 |
| 0 | 0 | 0 | 0 | | 0 | 0 | 0 | | |
| 0 | 1 | 0 | 0 | | 1 | 0 | 0 | | 30 |
| 0 | 0 | 0 | 0 | | 0 | 0 | 0 | | |
| 0 | 0 | 0 | 0 | | 0 | 0 | 0 | | |
| 0 | 0 | 0 | 0 | | 0 | 0 | 1 | | |
| 0 | 0 | 0 | 0 | | 1 | 0 | 0 | | |
| 0 | 0 | 1 | 0 | | 0 | 1 | 0 | | |
| 0 | 1 | 0 | 0 | | 1 | 0 | 0 | | |
| 0 | 0 | 1 | 1 | | 0 | 0 | 1 | | |
| 0 | 0 | 1 | 0 | | 0 | 0 | 1 | | |
| 0 | 1 | 0 | 0 | | 1 | 0 | 0 | | |
| 0 | 0 | 0 | 0 | | 0 | 0 | 0 | | |
| 0 | 0 | 0 | 0 | | 0 | 0 | 0 | | 15 |
| 0 | 0 | 0 | 0 | | 1 | 0 | 0 | | |
| 0 | 0 | 0 | 0 | | 1 | 0 | 0 | | |
| 0 | 1 | 0 | 0 | | 1 | 0 | 0 | | 15 |
| 1 | 0 | 0 | 0 | | 0 | 0 | 0 | | 15 |
| 1 | 0 | 0 | 0 | | 1 | 0 | 0 | | 10 |
| 0 | 0 | 0 | 0 | | 0 | 0 | 0 | | |
| 0 | 0 | 0 | 0 | | 1 | 0 | 0 | | 40 |